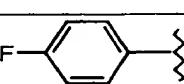
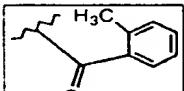
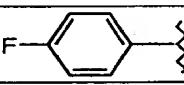
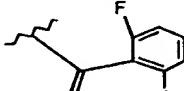
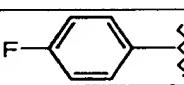
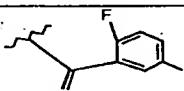
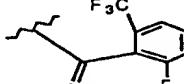
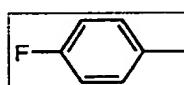
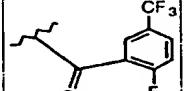
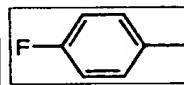
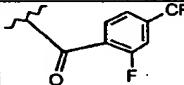
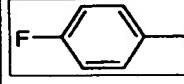
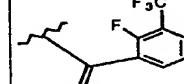
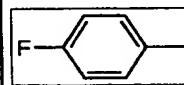
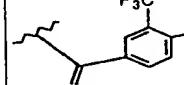
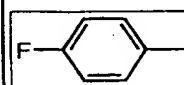
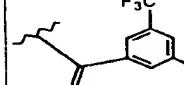
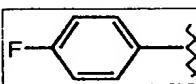
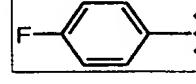
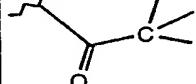
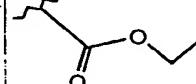
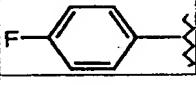
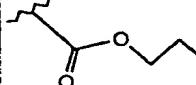
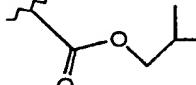
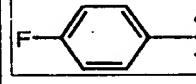
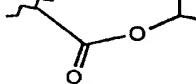
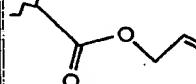
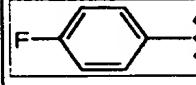
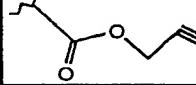
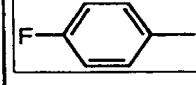
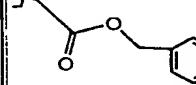
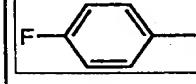
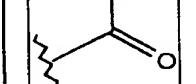
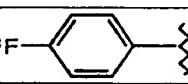
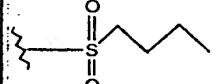
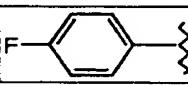
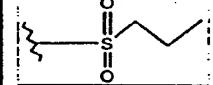
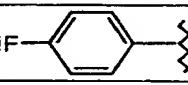
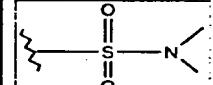
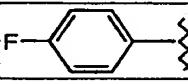
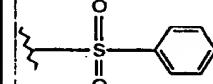
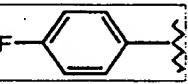
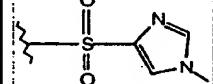
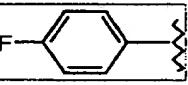
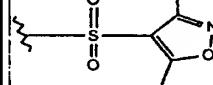
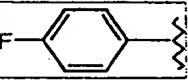
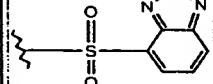


Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1400			74	440	441
B-1401			76	462	463
B-1402			65	462	463
B-1403			64	445	446
B-1404			70	512	513
B-1405			57	512	513
B-1406			73	512	513
B-1407			80	512	513
B-1408			2	512	513
B-1409			62	512	513

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1410			42	512	513
B-1411			19	462	463
B-1412			74	462	463
B-1413			75	494	495
B-1414			68	462	463
B-1415			48	462	463
B-1416			48	494	495
B-1417			57	494	495
B-1418			49	494	495
B-1419			39	494	495

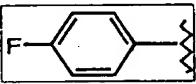
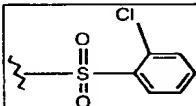
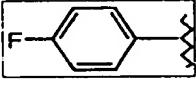
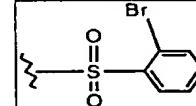
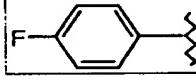
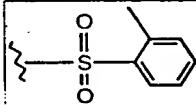
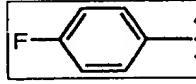
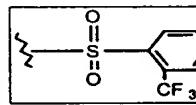
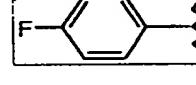
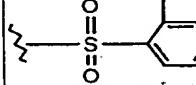
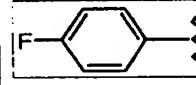
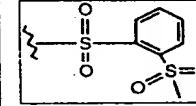
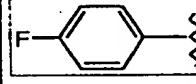
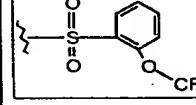
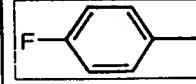
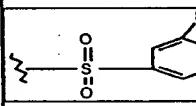
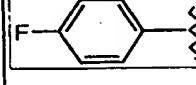
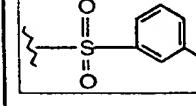
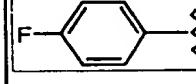
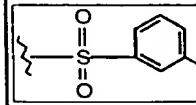
Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1420			72	378	379
B-1421			74	406	407
B-1422			68	394	395
B-1423			57	408	409
B-1424			77	422	423
B-1425			26	408	409
B-1426			41	406	407
B-1427			37	404	405
B-1428			60	456	457
B-1429			2	418	419

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Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1430			61	442	443
B-1431			64	428	429
B-1432			71	429	430
B-1433			74	462	463
B-1434			88	466	467
B-1435			75	481	482
B-1436			71	504	505

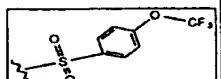
Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1437			63	468	469
B-1438			78	502	503
B-1439			70	545	546
B-1440			62	535	536
B-1441			82	608	
B-1442			79	555	556
B-1443			28	513	514
B-1444			75	522	523
B-1445			74	526	527
B-1446			70	570	571

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1447			73	506	507
B-1448			76	530	531
B-1449			82	530	531
B-1450			83	530	531
B-1451			74	530	531
B-1452			76	530	531
B-1453			73	530	531
B-1454			81	498	499
B-1455			83	498	499
B-1456			78	498	499

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1457			74	496	497
B-1458			82	540	541
B-1459			80	476	477
B-1460			78	530	531
B-1461			82	487	488
B-1462			71	540	541
B-1463			78	546	547
B-1464			83	480	481
B-1465			84	496	497
B-1466			80	540	541

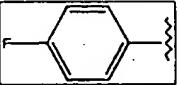
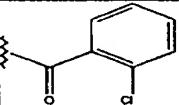
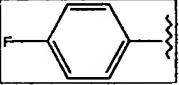
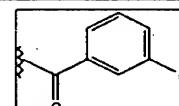
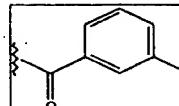
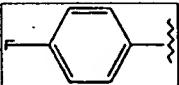
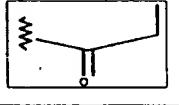
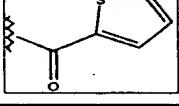
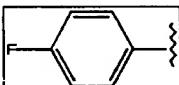
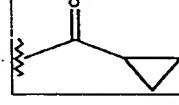
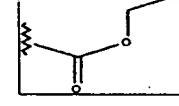
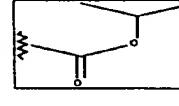
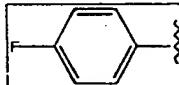
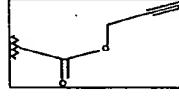
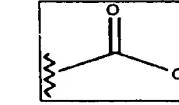
Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1467			79	476	477
B-1468			79	530	531
B-1469			75	487	488
B-1470			80	480	481
B-1471			74	496	497
B-1472			75	540	541
B-1473			77	476	477
B-1474			81	530	531
B-1475			70	487	488
B-1476			54	540	541

509

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1477			79	546	547

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1478			87	394	395
B-1479			41	504	505
B-1480			87	451	452
B-1481			18	416	417
B-1482			77	427	428
B-1483			74	406	407
B-1484			82	422	423

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1485			85	460	461
B-1486			64	406	407
B-1487			71	392	393
B-1488			82	427	428
B-1489			87	444	445
B-1490			81	462	463
B-1491			87	462	463
B-1492			69	364	365
B-1493			53	417	418
B-1494			17	426	427

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1495			79	460	461
B-1496			80	444	445
B-1497			82	460	461
B-1498			72	378	379
B-1499			70	432	433
B-1500			68	390	391
B-1501			63	394	395
B-1502			78	408	409
B-1503			55	404	405
B-1504			39	418	419

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1505			69	540	541
B-1506			69	462	463
B-1507			70	496	497
B-1508			65	480	481
B-1509			56	414	415
B-1510			62	400	401
B-1511			30	468	469
B-1512			50	476	477
B-1513			44	540	541
B-1514			42	530	531

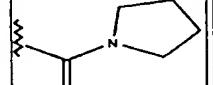
Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1515			68	496	497
B-1516			27	429	430
B-1517			92	466	467
B-1518			33	379	380
B-1519			50	393	394
B-1520			82	435	436
B-1521			86	509	510
B-1522			12	405	406
B-1523			59	459	460
B-1524			81	459	460

SUBSTITUTE SHEET (RULE 26)

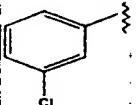
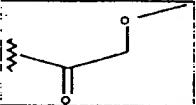
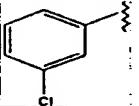
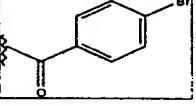
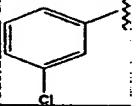
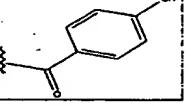
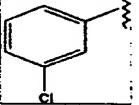
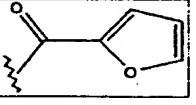
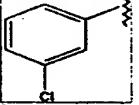
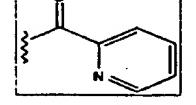
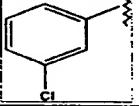
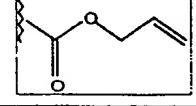
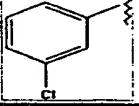
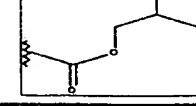
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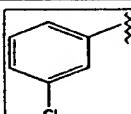
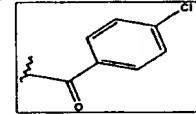
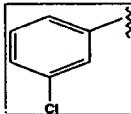
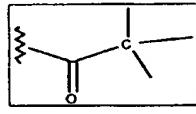
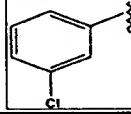
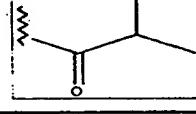
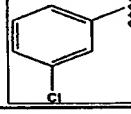
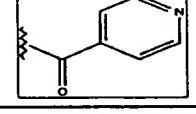
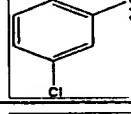
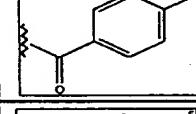
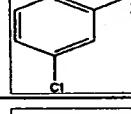
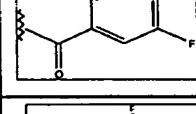
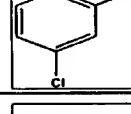
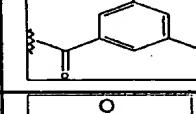
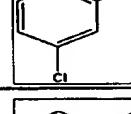
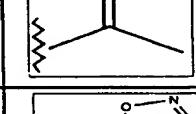
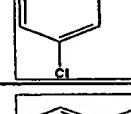
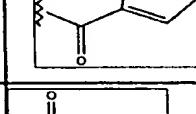
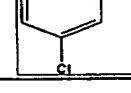
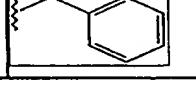
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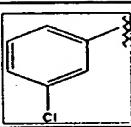
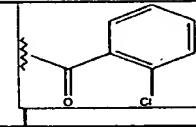
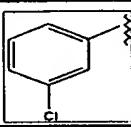
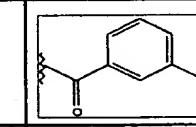
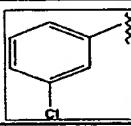
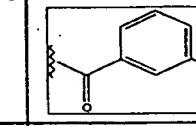
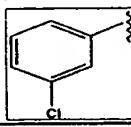
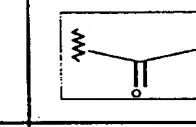
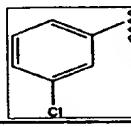
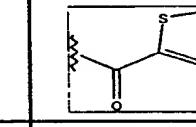
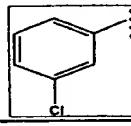
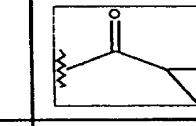
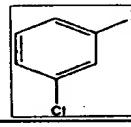
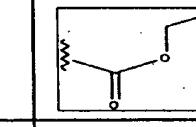
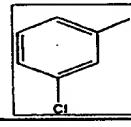
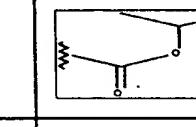
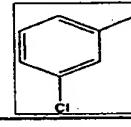
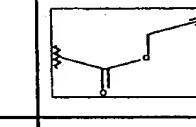
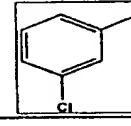
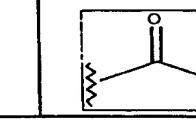
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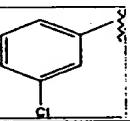
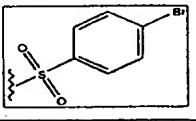
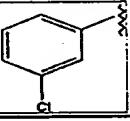
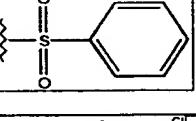
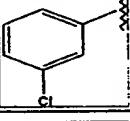
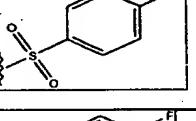
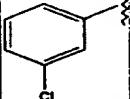
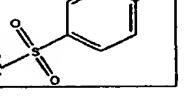
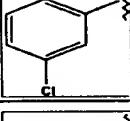
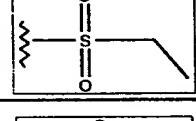
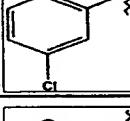
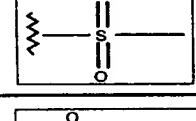
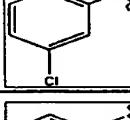
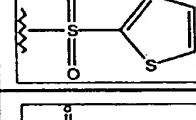
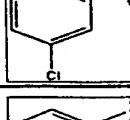
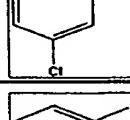
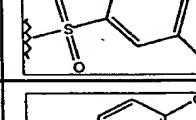
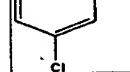
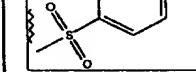
Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1525			57	419	420

SUBSTITUTE SHEET (RULE 26)

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1526			73	410	411
B-1527			66	520	521
B-1528			91	467	468
B-1529			73	432	433
B-1530			91	443	444
B-1531			74	422	423
B-1532			68	438	439

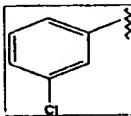
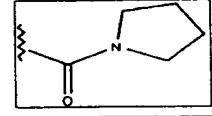
Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1533			84	476	477
B-1534			72	422	423
B-1535			78	408	409
B-1536			77	443	444
B-1537			86	460	461
B-1538			74	478	479
B-1539			85	478	479
B-1540			71	380	381
B-1541			71	433	434
B-1542			89	442	443

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1543			82	476	477
B-1544			76	460	461
B-1545			77	476	477
B-1546			76	394	395
B-1547			58	448	449
B-1548			83	406	407
B-1549			67	410	411
B-1550			37	424	425
B-1551			55	420	421
B-1552			23	434	435

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1553			83	556	557
B-1554			84	478	479
B-1555			93	512	513
B-1556			83	496	497
B-1557			62	430	431
B-1558			45	416	417
B-1559			67	484	485
B-1560			16	492	493
B-1561			84	556	557
B-1562			74	546	547

Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1563			72	512	513
B-1564			57	445	446
B-1565			64	482	483
B-1566			71	395	396
B-1567			54	409	410
B-1568			76	451	452
B-1569			70	525	526
B-1570			79	421	422
B-1571			60	475	476
B-1572			77	475	476

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Example#	R ²	R ^L	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1573			65	435	436

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Proton NMR data for selected members from Examples B-0001 through B-1573 are shown in the following table.

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Plate ID	1H NMR(solvent), d ppm
B-0120	(DMF-d7) d 8.53(brd, J = 4.99Hz, 2H), 7.44-7.24(m, 11H), 4.41(s, 2H), 4.31(br, 2H)
B-0224	(DMF-d7) d 8.56(brd, J = 4.98Hz, 2H), 7.78-7.69(m, 4H), 7.39-7.19(m, 6H), 4.23(br, 2H)
B-0235	(DMF-d7) d 8.47(br, 2H), 7.91-7.75(m, 3H), 7.57-7.53(m, 1H), 7.38-7.34(m, 2H), 7.21-7.13(m, 4H), 4.20(br, 2H)
B-0244	(CDCl3/CD3OD) d 8.38(d, J = 5.38 Hz, 1H), 7.62-7.32(m, 9H), 7.04-6.95(m, 4H), 6.86-6.80(m, 2H), 4.52(q, J = 6.96 Hz, 1H), 1.40(d, J = 6.88 Hz, 3H)
B-0256	(DMF-d7) d 8.45(brd, J = 2.85, 2H), 7.87(br s, 4H), 7.76-7.75(m, 2H), 7.53-7.33(m, 5H), 7.18-7.13(br, 4H)
B-0426	(DMF-d7), 1.32(br, 3H), 1.67(br, 3H), 4.17(br, 2H), 5.12(br, 1H), 7.50(m, 6H), 8.77(m, 2H), 13.54(br, 1H).
B-0438	(DMSO), 1.14(t, J = 6.9 Hz, 3H), 4.54(m, 1H), 6.99(br, 2H), 7.21(br, 4H), 7.45(s, 1H), 7.61(q, J = 8.7 Hz, 2H), 8.52(d, J = 5.2 Hz, 2H).
B-0466	(DMF-d7), 1.61(brd, J = 30.6 Hz, 3H), 4.61 (br, 1H), 7.25(m, 6H), 7.65(m, 3H), 8.59(br, 2H), 13.34(brd, J = 34.8 Hz, 1H).
B-0473	(CD3OD), 1.53(d, J = 7.2 Hz, 3H), 4.59(q, J = 7.2 Hz, 1H), 6.88(d, J = 4 Hz, 1H), 7.09(m, 3H), 7.15(dd, J = 4.4, 1.6 Hz, 2H), 7.26(m, 2H), 8.46(d, J = 6.0 Hz, 2H).
B-0477	(DMF), 1.80(br, 3H), 2.35(s, 1H), 4.98(br, 1H), 7.38(m, 6H), 7.85(m, 2H), 8.45(br, 1H), 8.75(d, J = 6.0 Hz, 2H).
B-0479	(Methanol-d4), 1.57(d, J = 5.6 Hz, 3H), 4.74(br, 1H), 7.23(m, 4H), 7.60(m, 2H), 7.81(m, 4H), 8.67(br, 2H).
B-0487	(DMF), 1.78(s, 3H), 2.76(br, 6H), 4.85(br, 1H), 7.42(br, 2H), 7.54(br, 2H), 7.66(br, 3H), 8.82(s, 2H).
B-0566	(CD3OD), 1.38(d, J = 7.2 Hz, 3H), 4.15(br, 2H), 4.50(br, 1H), 7.04(br, 2H), 7.18(br, 2H), 7.30(m, 7H), 8.45(m, 2H).
B-0569	(CD3OD), 1.56(br, 3H), 4.66(q, J = 6.7 Hz, 1H), 7.17(m, 8H), 7.56(m, 2H), 8.47(s, 2H).
B-0574	(Methanol-d4), 1.49(br, 3H), 3.86(br, 3H), 4.60(br, 1H), 6.92(br, 2H), 7.19(br, 2H), 7.31(br, 2H), 7.76(m, 4H), 8.60(br, 2H).
B-0639	(DMF-d7), 1.58(brd, J = 30.0 Hz, 3H), 4.62(br, 1H), 7.25(m, 6H), 7.60(m, 4H), 8.59(br, 2H), 13.30(brd, J = 12.3 Hz).
B-0643	7.18(m, 2H), 7.32(dd, J = 6.0, 4.4 Hz, 1H), 7.70(dd, J = 9.0, 5.8Hz, 1H), 8.43(dd, J = 4.8, 3.2 Hz, 2H).
B-0650	(CD3OD), 1.58(br, 3H), 4.62(q, J = 6.6 Hz, 1H), 6.93(br, 1H), 7.17(m, 5H), 7.31(br, 2H), 8.51(br, 2H).
B-0656	(CDCl3/CD3OD) d 8.48 (d, J = 5.30 Hz, 2H), 7.72-7.59(m, 4H), 7.14-7.10(m, 2H), 7.03-6.97(m, 4H), 4.60(q, J = 7.57Hz, 1H), 1.43(d, J = 7.26Hz, 3H)
B-0663	(CD3OD), 1.52(d, J = 6.8 Hz, 3H), 3.75(s, 3H), 7.21(m, 2H), 7.42(m, 2H), 7.57(s, 1H), 7.76(s, 1H), 7.98(br, 2H), 8.76(br, 2H).
B-1165	Hz, 2H), 3.06(m, 1H), 3.43(q, J = 6.1 Hz, 2H), 7.02(m, 2H), 7.14(m, 2H), 7.41(m, 2H), 8.59(d, J = 5.6 Hz, 2H).
B-1169	= 1.6 Hz, 1H), 7.04(t, J = 8.6 Hz, 2H), 7.14(m, 2H), 7.36(m, 2H), 8.39(d, J = 1.8 Hz, 1H), 8.60(m, 2H).
B-1171	6.83(br, 1H), 7.02(t, J = 8.7 Hz, 2H), 7.15(d, J = 5.6 Hz, 2H), 7.40(m, 2H), 8.59(d, J = 5.0 Hz, 2H).

Plate ID	1H NMR(solvent), d ppm
B-1179	(CDCl3), 1.94(br, 2H), 2.53(s, 3H), 2.85(t, J = 6.2 Hz, 2H), 3.65(br, 2H), 6.15(br, 1H), 7.04(m, 3H), 7.22(m, 3H), 7.41(br, 4H), 8.60(br, 2H).
B-1183	(CDCl3), 2.00(br, 2H), 2.85(br, 2H), 3.64(br, 2H), 7.03(br, 3H), 7.17(br, 2H), 7.36(br, 2H), 7.66(br, 2H), 8.60(br, 2H), 8.77(br, 2H).
B-1194	(DMSO), 1.76(br, 2H), 2.66(br, 2H), 2.91(br, 2H), 4.30(s, 2H), 7.18(br, 5H), 7.35(m, 6H), 8.54(d, J = 5.8 Hz, 2H).
B-1200	(DMSO), 1.17(br, 3H), 1.76(br, 2H), 2.71(br, 2H), 2.97(br, 4H), 7.18(br, 4H), 7.36(br, 2H), 8.54(br, 2H).
B-1206	(DMSO), 1.03(s, 6H), 1.68(br, 2H), 2.63(br, 2H), 3.00(br, 2H), 3.65(br, 1H), 5.69(m, 2H), 7.16(br, 4H), 7.35(br, 2H), 8.54(br, 2H).
B-1216	(DMSO), 1.75(m, 2H), 2.14(s, 6H), 2.66(br, 2H), 3.10(br, 2H), 7.04(br, 3H), 7.18(br, 4H), 7.35(m, 2H), 7.47(br, 1H), 8.54(d, J = 4.8 Hz, 2H).
B-1226	(DMF), 1.25(br, 3H), 2.01(br, 2H), 3.35(br, 4H), 6.20(s, 1H), 6.30(s, 1H), 7.42(br, 4H), 7.65(br, 2H), 8.77(s, 2H).
B-1360	(DMSO-d6), 1.80(br, 4H), 2.82(br, 1H), 2.94(br, 1H), 3.10(br, 1H), 3.60(br, 1H), 4.54(br, 1H), 7.18(m, 4H), 7.30(m, 4H), 7.46(m, 2H), 8.54(br, 2H).
B-1361	(DMSO-d6), 0.99(br, 6H), 1.73(br, 4H), 2.89(br, 2H), 3.03(m, 1H), 4.04(br, 2H), 4.44(m, 1H), 7.18(m, 4H), 7.30(m, 2H), 8.57(d, J = 4.64 Hz, 2H).
B-1363	(DMSO-d6), 1.78(br, 4H), 2.01(s, 3H), 2.89(br, 1H), 3.05(br, 1H), 3.34(br, 1H), 3.85(br, 1H), 4.48(br, 1H), 7.12(br, 2H), 7.21(br, 2H), 7.30(br, 2H), 8.69(br, 2H).
B-1364	(CDCl3), 0.78(dd, J = 3.0, 2.9 Hz, 2H), 1.00(s, 2H), 1.78(m, 1H), 1.86(b, 4H), 2.64(m, 1H), 2.99(m, 1H), 3.16(m, 1H), 4.33(br, 1H), 4.70(br, 1H), 6.99(m, 2H), 7.14(s, 2H), 7.29(m, 2H), 8.64(s, 2H).
B-1368	(CDCl3), 1.89(s, 4H), 2.65(m, 1H), 2.96(m, 1H), 3.06(m, 1H), 3.43(s, 3H), 3.93(d, J = 13.2 Hz, 1H), 4.09(d, J = 13.5 Hz, 1H), 4.18(d, J = 13.5 Hz, 1H), 4.68(d, J = 12.4 Hz, 1H), 7.60(m, 2H), 7.12(s, 2H), 7.26(m, 2H), 8.63(s, 2H).

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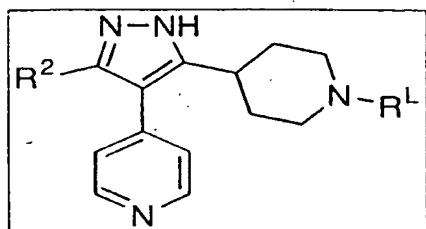
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By analogy to the procedure identified above for the preparation of Examples B0001-B0048, the following
15 examples B-1574 through B-2269 are prepared.

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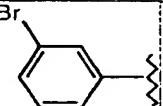
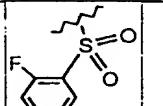
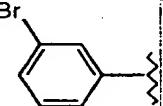
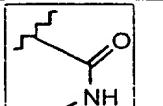
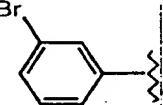
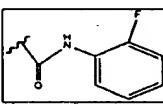
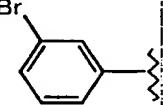
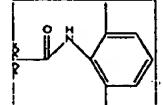
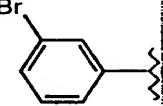
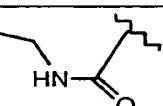
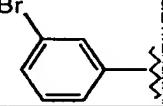
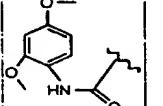
Examples B-1574 through B-1597 are prepared from Scaffold C-27

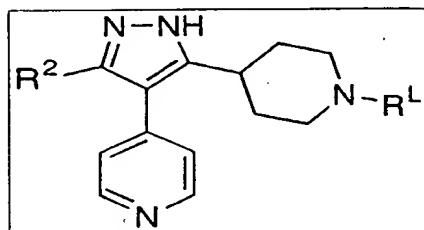
Example#

 R^2 R^1

B-1574						
B-1575						
B-1576						
B-1577						
B-1578						
B-1579						
B-1580						

B-1581						
B-1582						
B-1583						
B-1584						
B-1585						
B-1586						
B-1587						
B-1588						
B-1589						
B-1590						
B-1591						

B-1592						
B-1593						
B-1594						
B-1595						
B-1596						
B-1597						



Examples B-1598 through B-1621 are prepared from Scaffold C-28

Example#

R²R^L

B-1598					
B-1599					
B-1600					
B-1601					
B-1602					
B-1603					
B-1604					

Example#

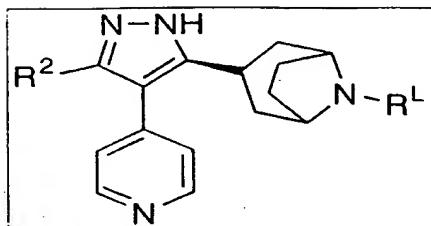
 R^2 R^L

B-1605						
B-1606						
B-1607						
B-1608						
B-1609						
B-1610						
B-1611						
B-1612						
B-1613						
B-1614						

Example#

 R^2 R^L

B-1615					
B-1616					
B-1617					
B-1618					
B-1619					
B-1620					
B-1621					

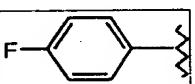
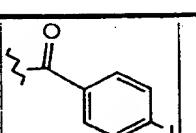
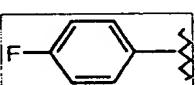
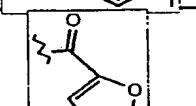
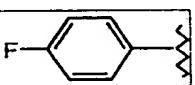
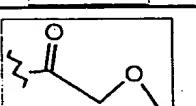
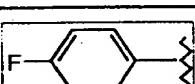
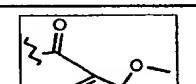
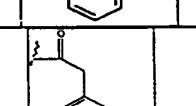
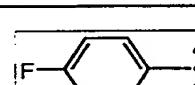
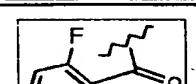
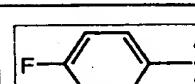
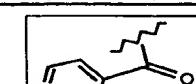
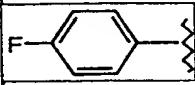
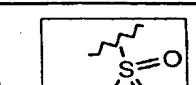


Examples B-1622 through B-1645 are prepared from Scaffold C-38

Example#	R^2	R^L				
B-1622						
B-1623						
B-1624						
B-1625						
B-1626						
B-1627						
B-1628						

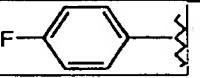
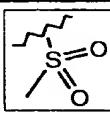
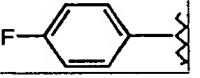
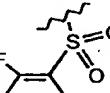
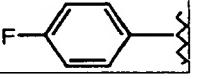
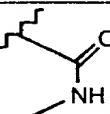
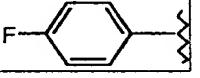
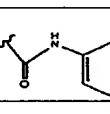
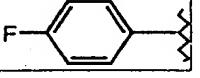
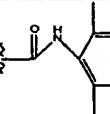
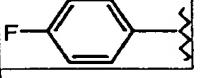
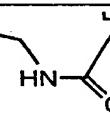
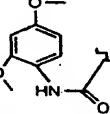
Example#

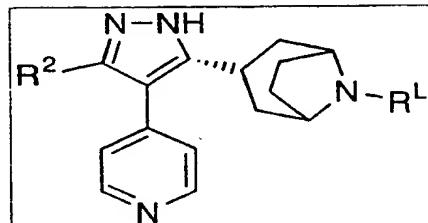
 R^2 R^L

B-1629					
B-1630					
B-1631					
B-1632					
B-1633					
B-1634					
B-1635					
B-1636					
B-1637					
B-1638					

Example#

 R^2 R^L

B-1639					
B-1640					
B-1641					
B-1642					
B-1643					
B-1644					
B-1645					



Examples B-1646 through B-1669 are prepared from Scaffold C-39

Example#

 R^2 R^L

B-1646					
B-1647					
B-1648					
B-1649					
B-1650					
B-1651					
B-1652					

SUBSTITUTE SHEET (RULE 26)

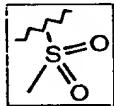
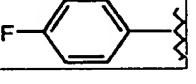
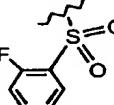
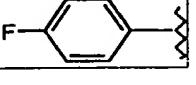
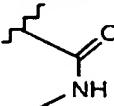
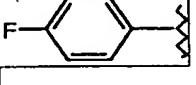
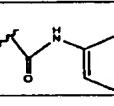
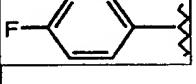
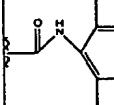
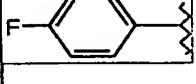
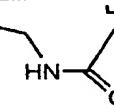
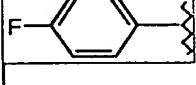
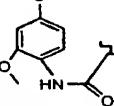
Example#

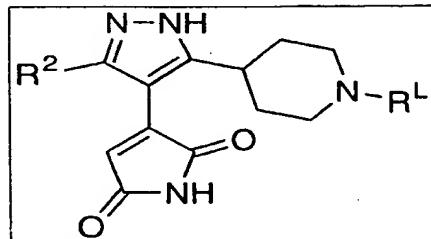
 R^2 R^L

B-1653						
B-1654						
B-1655						
B-1656						
B-1657						
B-1658						
B-1659						
B-1660						
B-1661						
B-1662						

Example#

 R^2 R^L

B-1663					
B-1664					
B-1665					
B-1666					
B-1667					
B-1668					
B-1669					

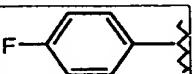
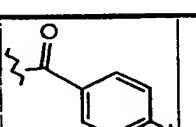
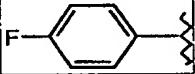
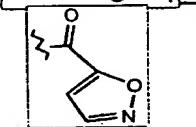
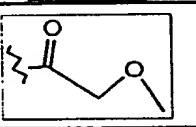
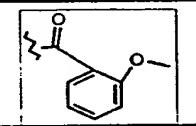
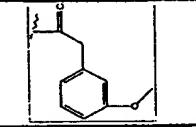
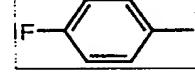
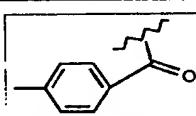
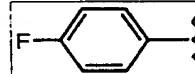
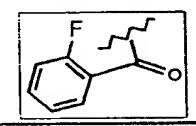
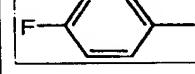
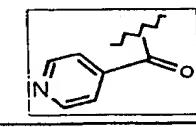
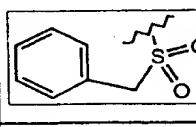
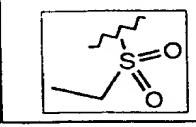


Examples B-1670 through B-1693 are prepared from Scaffold C-65

Example#

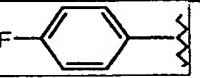
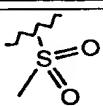
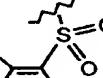
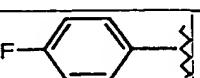
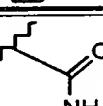
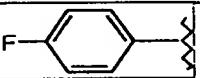
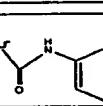
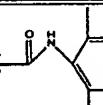
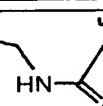
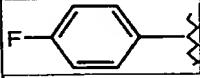
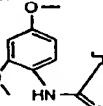
 R^2 R^L

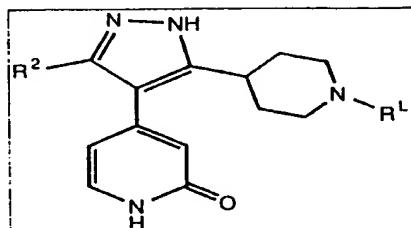
B-1670					
B-1671					
B-1672					
B-1673					
B-1674					
B-1675					
B-1676					

Example#	R ²	R ^L				
B-1677						
B-1678						
B-1679						
B-1680						
B-1681						
B-1682						
B-1683						
B-1684						
B-1685						
B-1686						

Example#

 R^2 R^L

B-1687					
B-1688					
B-1689					
B-1690					
B-1691					
B-1692					
B-1693					



Examples B-1694 through B-1717 are prepared from Scaffold C-66

Example#

 R^2 R^L

B-1694					
B-1695					
B-1696					
B-1697					
B-1698					
B-1699					
B-1700					

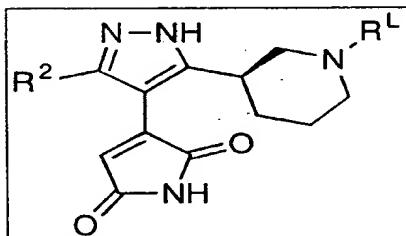
SUBSTITUTE SHEET (RULE 26)

Example#

 R^2 R^L

B-1701					
B-1702					
B-1703					
B-1704					
B-1705					
B-1706					
B-1707					
B-1708					
B-1709					
B-1710					

Example#	R ²	R ^L				
B-1711						
B-1712						
B-1713						
B-1714						
B-1715						
B-1716						
B-1717						



Examples B-1718 through B-1741 are prepared from Scaffold C-69

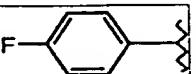
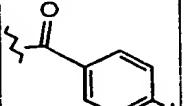
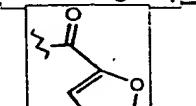
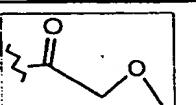
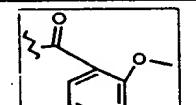
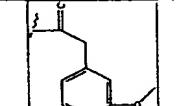
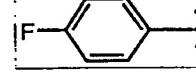
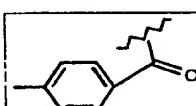
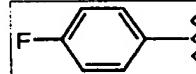
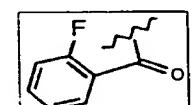
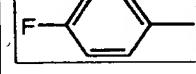
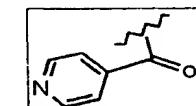
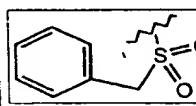
Example#

 R^2 R^L

B-1718					
B-1719					
B-1720					
B-1721					
B-1722					
B-1723					
B-1724					

Example#

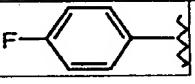
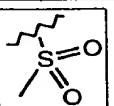
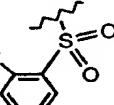
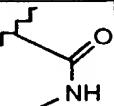
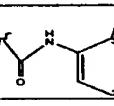
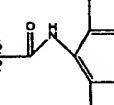
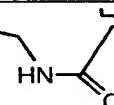
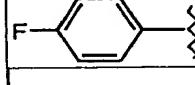
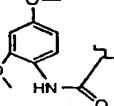
 R^2 R^L

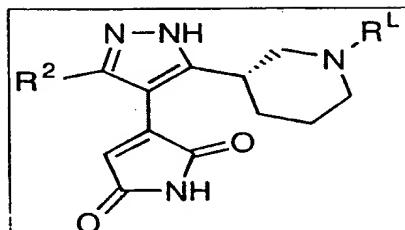
B-1725					
B-1726					
B-1727					
B-1728					
B-1729					
B-1730					
B-1731					
B-1732					
B-1733					
B-1734					

SUBSTITUTE SHEET (RULE 26)

Example#

 R^2 R^L

B-1735					
B-1736					
B-1737					
B-1738					
B-1739					
B-1740					
B-1741					

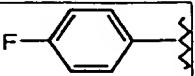
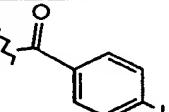
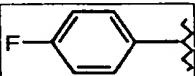
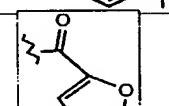
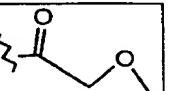
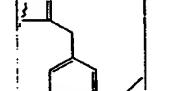
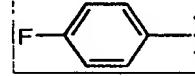
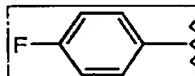
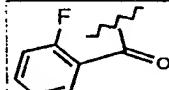
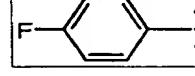
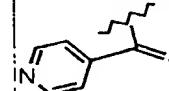
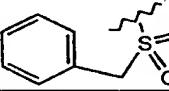


Examples B-1742 through B-1765 are prepared from Scaffold C-70

Example#

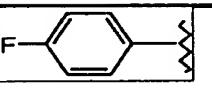
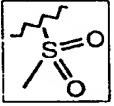
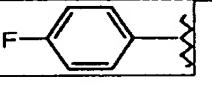
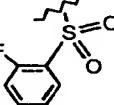
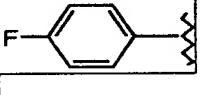
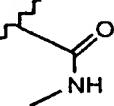
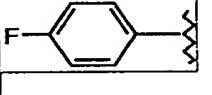
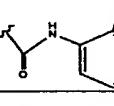
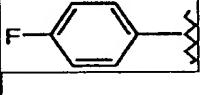
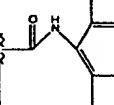
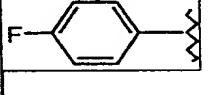
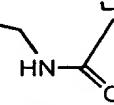
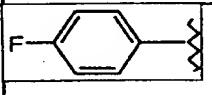
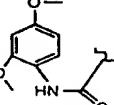
 R^2 R^L

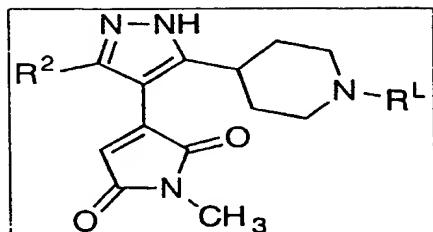
B-1742					
B-1743					
B-1744					
B-1745					
B-1746					
B-1747					
B-1748					

Example#	R ²	R ^L				
B-1749						
B-1750						
B-1751						
B-1752						
B-1753						
B-1754						
B-1755						
B-1756						
B-1757						
B-1758						

Example#

 R^2 R^L

B-1759					
B-1760					
B-1761					
B-1762					
B-1763					
B-1764					
B-1765					

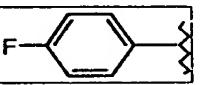
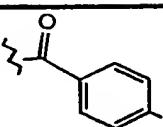
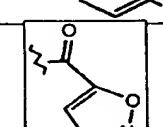
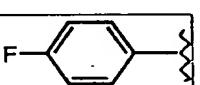
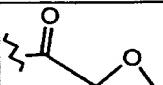
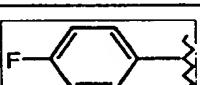
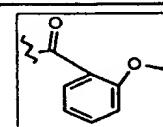
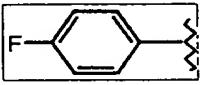
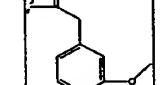
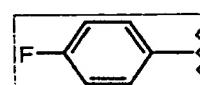
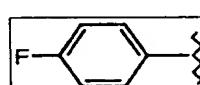
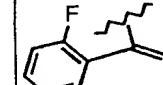
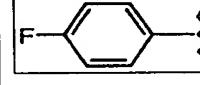
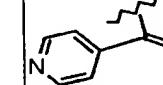
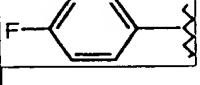
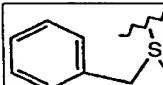
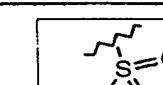


Examples B-1766 through B-1789 are prepared from Scaffold C-71

Example#

 R^2 R^L

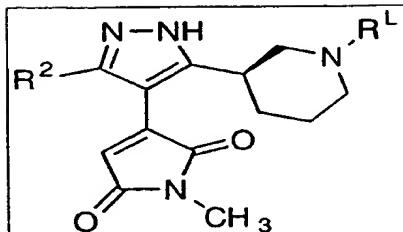
B-1766						
B-1767						
B-1768						
B-1769						
B-1770						
B-1771						
B-1772						

Example#	R^2	R^L				
B-1773						
B-1774						
B-1775						
B-1776						
B-1777						
B-1778						
B-1779						
B-1780						
B-1781						
B-1782						

Example#

 R^2 R^1

B-1783					
B-1784					
B-1785					
B-1786					
B-1787					
B-1788					
B-1789					



Examples B-1790 through B-1813 are prepared from Scaffold C-72

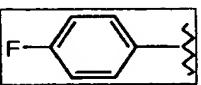
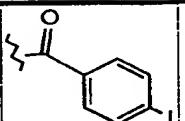
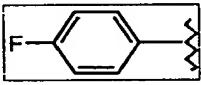
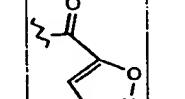
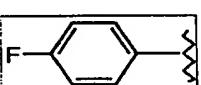
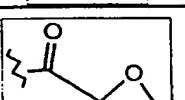
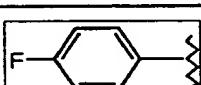
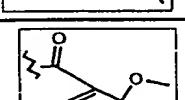
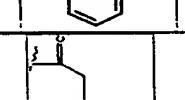
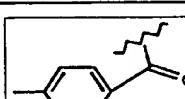
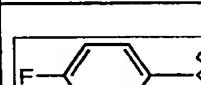
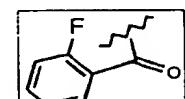
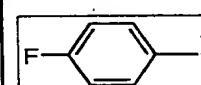
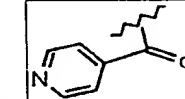
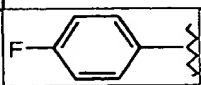
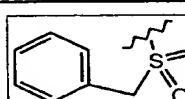
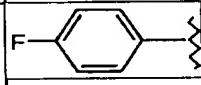
Example#

*R*²*R*^L

B-1790					
B-1791					
B-1792					
B-1793					
B-1794					
B-1795					
B-1796					

Example#

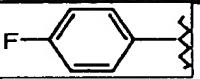
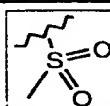
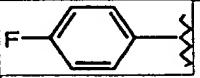
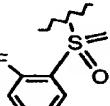
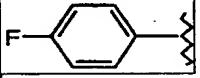
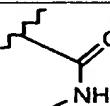
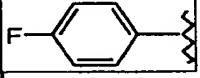
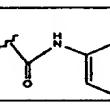
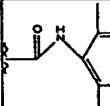
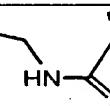
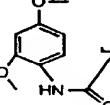
 R^2 R^L

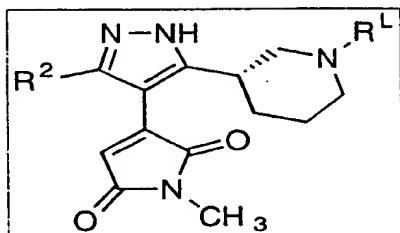
B-1797					
B-1798					
B-1799					
B-1800					
B-1801					
B-1802					
B-1803					
B-1804					
B-1805					
B-1806					

SUBSTITUTE SHEET (RULE 26)

Example#

 R^2 R^L

B-1807					
B-1808					
B-1809					
B-1810					
B-1811					
B-1812					
B-1813					



Examples B-1814 through B-1837 are prepared from Scaffold C-73

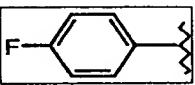
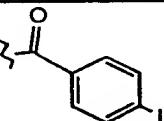
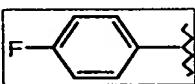
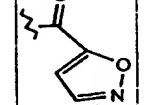
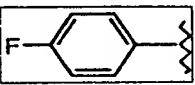
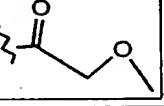
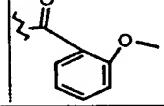
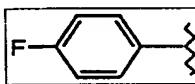
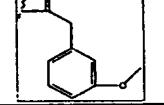
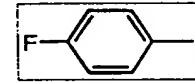
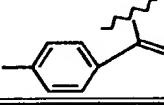
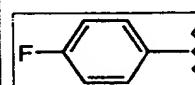
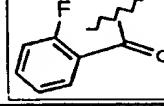
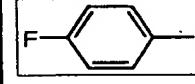
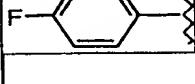
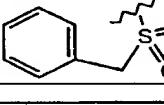
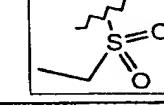
Example#

 R^2 R^L

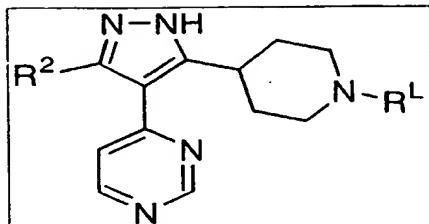
B-1814					
B-1815					
B-1816					
B-1817					
B-1818					
B-1819					
B-1820					

Example#

 R^2 R^L

B-1821					
B-1822					
B-1823					
B-1824					
B-1825					
B-1826					
B-1827					
B-1828					
B-1829					
B-1830					

Example#	R^2	R^L			
B-1831					
B-1832					
B-1833					
B-1834					
B-1835					
B-1836					
B-1837					

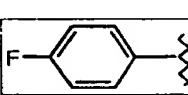
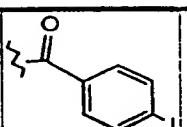
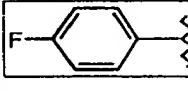
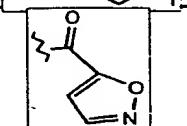
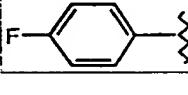
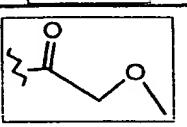
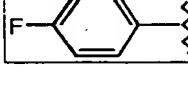
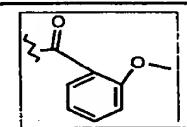
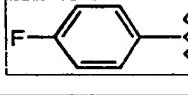
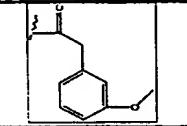
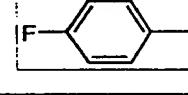
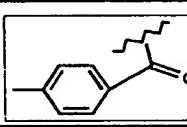
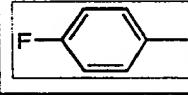
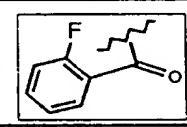
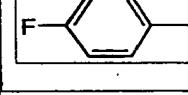
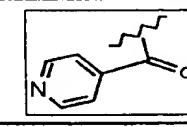
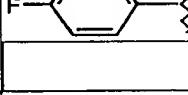
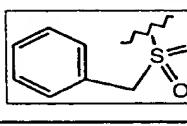
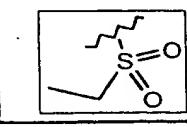


Examples B-1838 through B-1861 are prepared from Scaffold C-33

Example#

 R^2 R^L

B-1838					
B-1839					
B-1840					
B-1841					
B-1842					
B-1843					
B-1844					

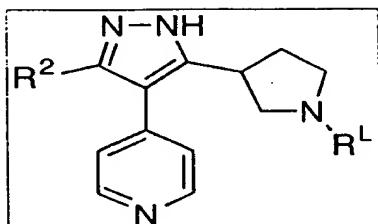
Example#	R^2	R^L				
B-1845						
B-1846						
B-1847						
B-1848						
B-1849						
B-1850						
B-1851						
B-1852						
B-1853						
B-1854						

Example#

 R^2 R^L

B-1855					
B-1856					
B-1857					
B-1858					
B-1859					
B-1860					
B-1861					

SUBSTITUTE SHEET (RULE 26)

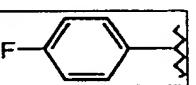
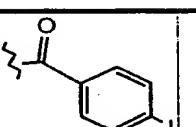
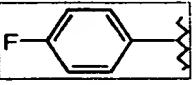
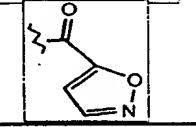
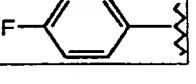
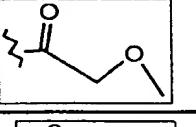
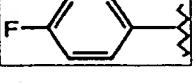
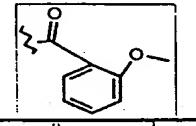
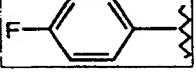
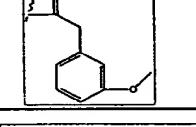
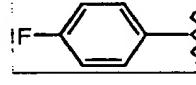
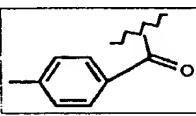
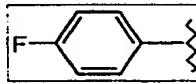
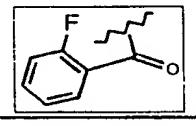
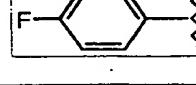
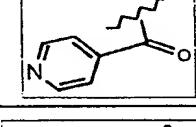
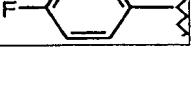
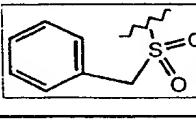
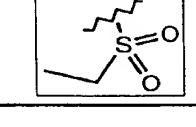


Examples B-1862 through B-1885 are prepared from Scaffold C-45

Example#	R^2	R^L			
B-1862					
B-1863					
B-1864					
B-1865					
B-1866					
B-1867					
B-1868					

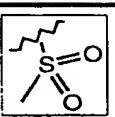
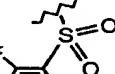
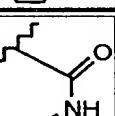
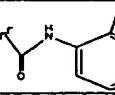
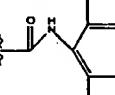
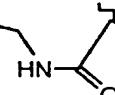
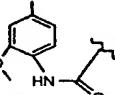
Example#

 R^2 R^L

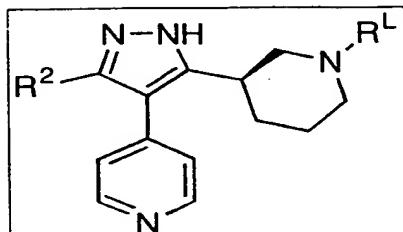
B-1869					
B-1870					
B-1871					
B-1872					
B-1873					
B-1874					
B-1875					
B-1876					
B-1877					
B-1878					

Example#

 R^2 R^L

B-1879					
B-1880					
B-1881					
B-1882					
B-1883					
B-1884					
B-1885					

SUBSTITUTE SHEET (RULE 26)



Examples B-1886 through B-1909 prepared from Scaffold C-42

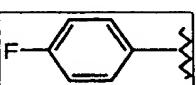
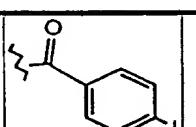
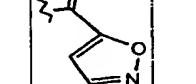
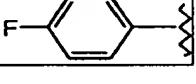
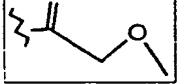
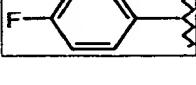
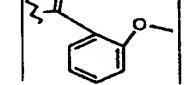
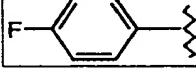
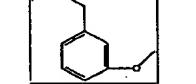
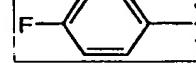
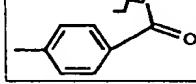
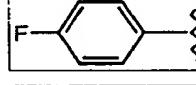
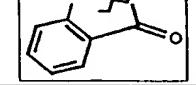
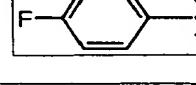
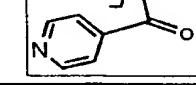
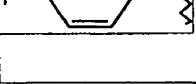
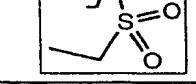
Example#

 R^2 R^L

B-1886					
B-1887					
B-1888					
B-1889					
B-1890					
B-1891					
B-1892					

Example#

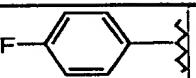
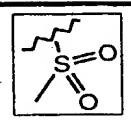
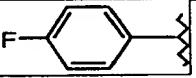
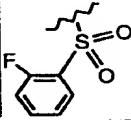
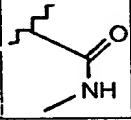
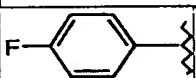
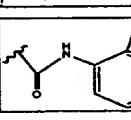
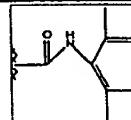
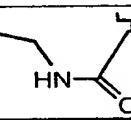
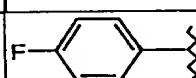
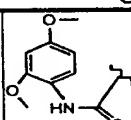
 R^2 R^L

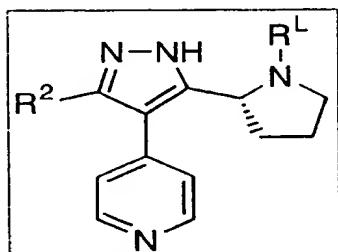
B-1893						
B-1894						
B-1895						
B-1896						
B-1897						
B-1898						
B-1899						
B-1900						
B-1901						
B-1902						

SUBSTITUTE SHEET (RULE 26)

Example#

 R^2 R^L

B-1903						
B-1904						
B-1905						
B-1906						
B-1907						
B-1908						
B-1909						

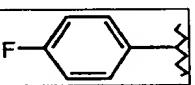
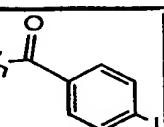
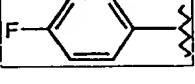
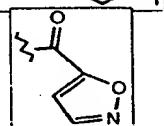
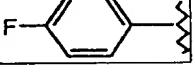
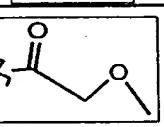
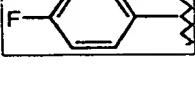
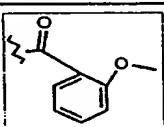
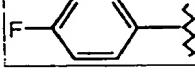
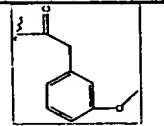
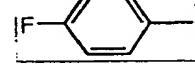
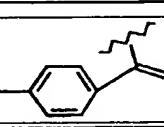
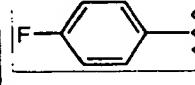
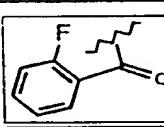
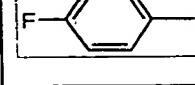
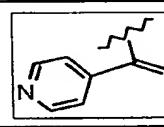
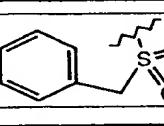
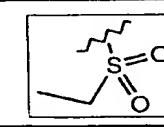


Examples B-1910 through B-1933 are prepared from Scaffold C-44

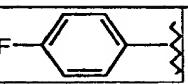
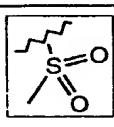
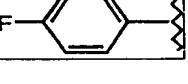
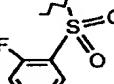
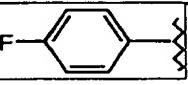
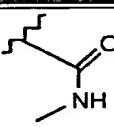
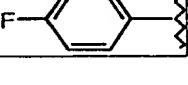
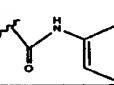
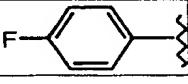
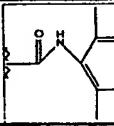
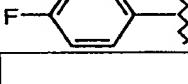
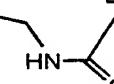
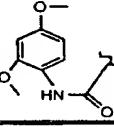
Example#

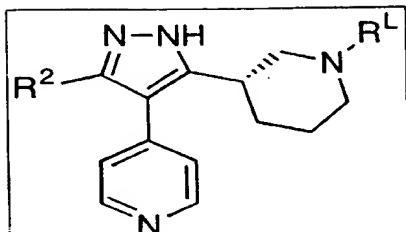
R²R^L

B-1910					
B-1911					
B-1912					
B-1913					
B-1914					
B-1915					
B-1916					

Example#	R ²	R ^L				
B-1917						
B-1918						
B-1919						
B-1920						
B-1921						
B-1922						
B-1923						
B-1924						
B-1925						
B-1926						

SUBSTITUTE SHEET (RULE 26)

Example#	R ²	R ^L			
B-1927					
B-1928					
B-1929					
B-1930					
B-1931					
B-1932					
B-1933					



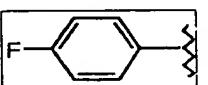
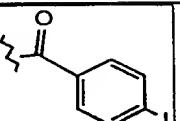
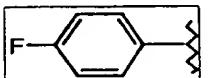
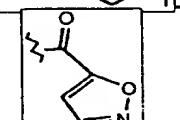
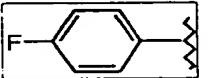
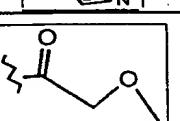
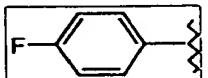
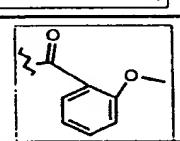
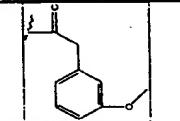
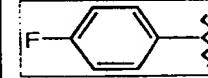
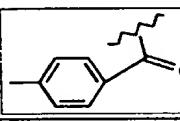
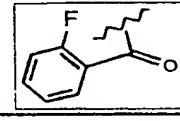
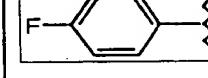
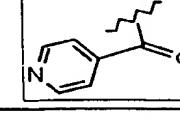
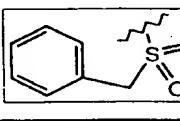
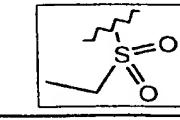
Examples B-1934 through B-1957 are prepared from Scaffold C-41

Example#

 R^2 R^L

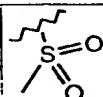
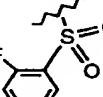
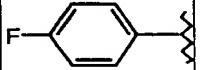
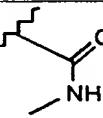
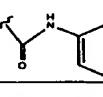
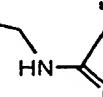
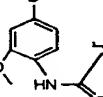
B-1934					
B-1935					
B-1936					
B-1937					
B-1938					
B-1939					
B-1940					

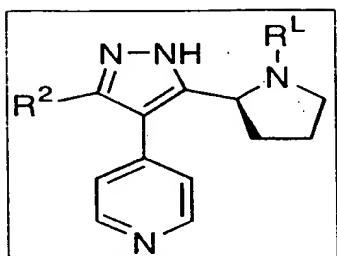
SUBSTITUTE SHEET (RULE 26)

Example#	R^2	R^L				
B-1941						
B-1942						
B-1943						
B-1944						
B-1945						
B-1946						
B-1947						
B-1948						
B-1949						
B-1950						

Example#

 R^2 R^L

B-1951					
B-1952					
B-1953					
B-1954					
B-1955					
B-1956					
B-1957					



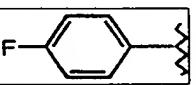
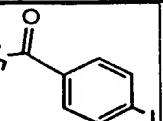
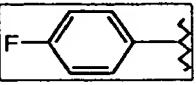
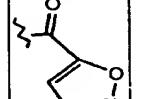
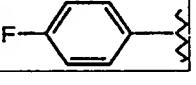
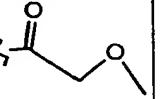
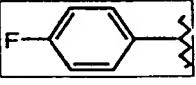
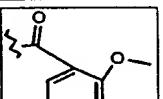
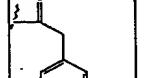
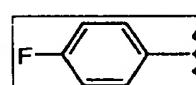
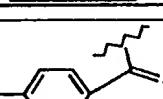
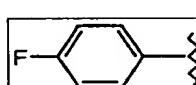
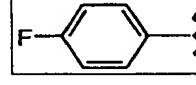
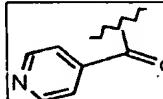
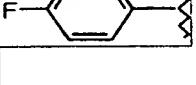
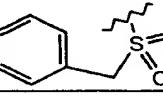
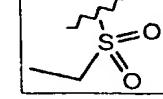
Examples B-1958 through B-1981 are prepared from Scaffold C-43

Example# R² R^L

B-1958					
B-1959					
B-1960					
B-1961					
B-1962					
B-1963					
B-1964					

Example#

 R^2 R^L

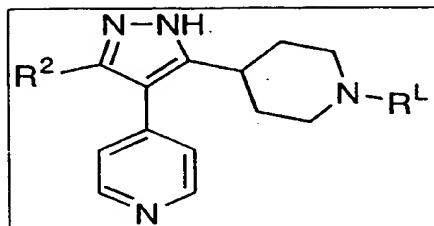
B-1965					
B-1966					
B-1967					
B-1968					
B-1969					
B-1970					
B-1971					
B-1972					
B-1973					
B-1974					

SUBSTITUTE SHEET (RULE 26)

Example#

 R^2 R^L

B-1975					
B-1976					
B-1977					
B-1978					
B-1979					
B-1980					
B-1981					



Examples B-1982 through B-2005 are prepared from Scaffold C-30

Example#

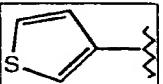
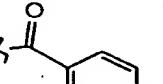
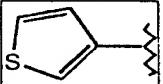
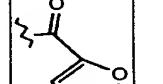
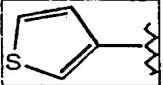
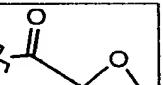
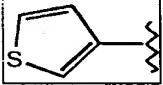
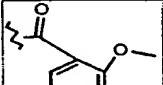
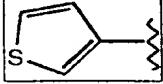
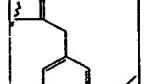
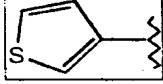
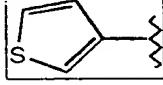
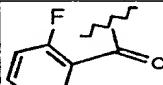
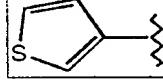
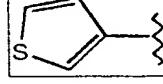
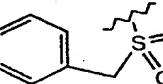
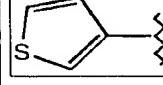
 R^2 R^L

B-1982					
B-1983					
B-1984					
B-1985					
B-1986					
B-1987					
B-1988					

SUBSTITUTE SHEET (RULE 26)

Example#

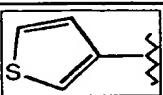
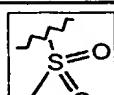
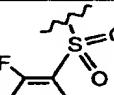
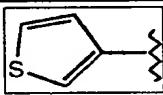
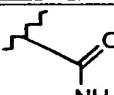
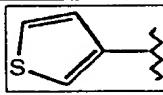
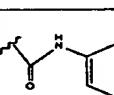
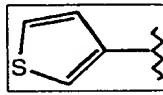
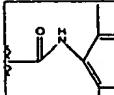
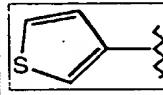
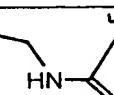
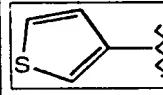
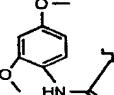
 R^2 R^L

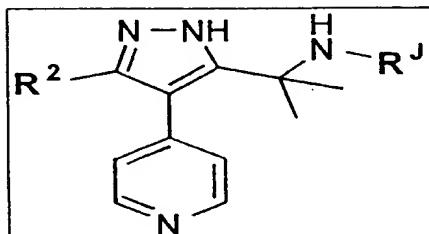
B-1989					
B-1990					
B-1991					
B-1992					
B-1993					
B-1994					
B-1995					
B-1996					
B-1997					
B-1998					

SUBSTITUTE SHEET (RULE 26)

Example#

 R^2 R^L

B-1999					
B-2000					
B-2001					
B-2002					
B-2003					
B-2004					
B-2005					

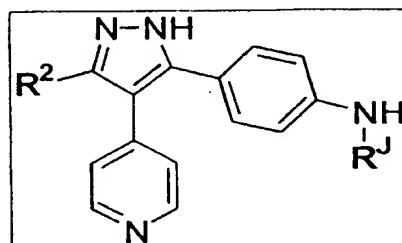


Examples B-2006 through B-2029 are prepared from Scaffold C-60

Example#	R^2	R^j			
B-2006					
B-2007					
B-2008					
B-2009					
B-2010					
B-2011					
B-2012					

Example#	R ²	R ⁴			
B-2013					
B-2014					
B-2015					
B-2016					
B-2017					
B-2018					
B-2019					
B-2020					
B-2021					
B-2022					

Example#	R ²	R ¹			
B-2023					
B-2024					
B-2025					
B-2026					
B-2027					
B-2028					
B-2029					

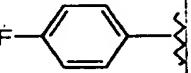
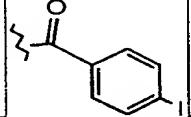
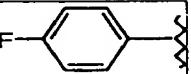
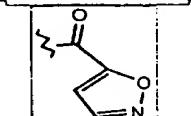
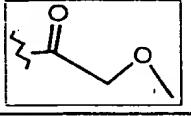
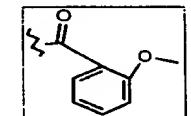
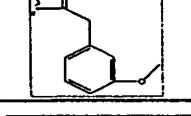
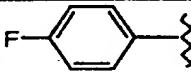
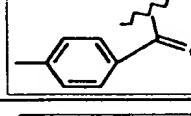
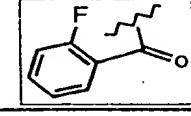
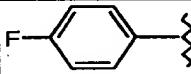
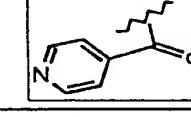
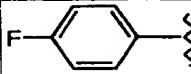
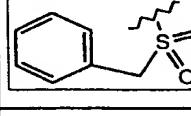
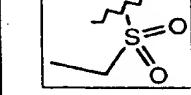


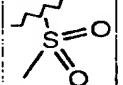
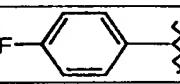
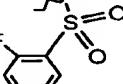
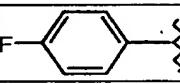
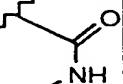
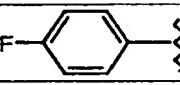
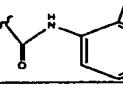
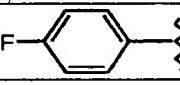
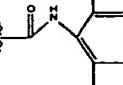
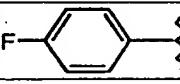
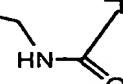
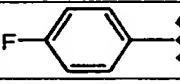
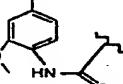
Examples B-2030 through B-2053 are prepared from Scaffold C-36

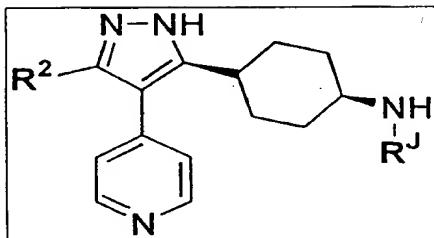
Example#	R^2	R^J			
B-2030					
B-2031					
B-2032					
B-2033					
B-2034					
B-2035					
B-2036					

Example#

 R^2 R^4

B-2037					
B-2038					
B-2039					
B-2040					
B-2041					
B-2042					
B-2043					
B-2044					
B-2045					
B-2046					

Example#	R ²	R ¹			
B-2047					
B-2048					
B-2049					
B-2050					
B-2051					
B-2052					
B-2053					



Examples B-2054 through B-2077 are prepared from Scaffold C-34

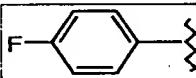
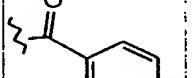
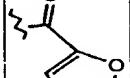
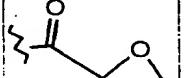
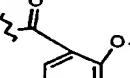
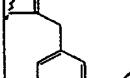
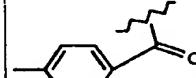
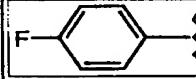
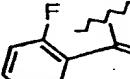
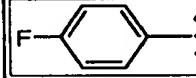
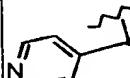
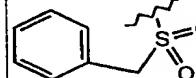
Example#

 R^2 R^J

B-2054					
B-2055					
B-2056					
B-2057					
B-2058					
B-2059					
B-2060					

Example#

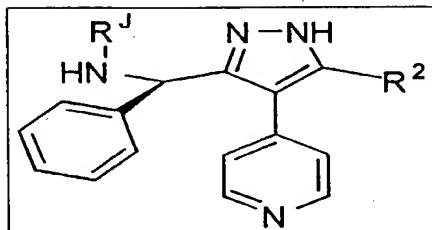
 R^2 R^J

B-2061					
B-2062					
B-2063					
B-2064					
B-2065					
B-2066					
B-2067					
B-2068					
B-2069					
B-2070					

Example#

 R^2 R^4

B-2071					
B-2072					
B-2073					
B-2074					
B-2075					
B-2076					
B-2077					



Examples B-2078 through B-2101 are prepared from Scaffold C-57

Example#	R^2	R^1			
B-2078					
B-2079					
B-2080					
B-2081					
B-2082					
B-2083					
B-2084					

SUBSTITUTE SHEET (RULE 28)

Example#

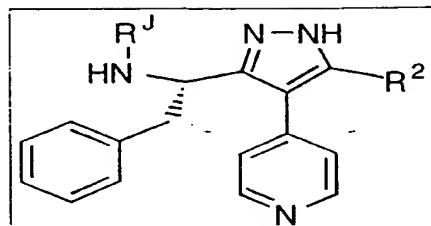
 R^2 R^J

B-2085					
B-2086					
B-2087					
B-2088					
B-2089					
B-2090					
B-2091					
B-2092					
B-2093					

Example#

 R^2 R^J

B-2094					
B-2095					
B-2096					
B-2097					
B-2098					
B-2099					
B-2100					
B-2101					



Examples B-2102 through B-2125 are prepared from Scaffold C-52

Example#

 R^2 R^1

B-2102					
B-2103					
B-2104					
B-2105					
B-2106					
B-2107					
B-2108					

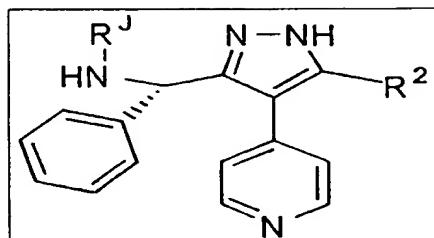
SUBSTITUTE SHEET (RULE 28)

Example#	R ²	R ^J			
B-2109					
B-2110					
B-2111					
B-2112					
B-2113					
B-2114					
B-2115					
B-2116					
B-2117					
B-2118					

Example#

 R^2 R^J

B-2119					
B-2120					
B-2121					
B-2122					
B-2123					
B-2124					
B-2125					



Examples B-2126 through B-2149 are prepared from Scaffold C-56

Example#

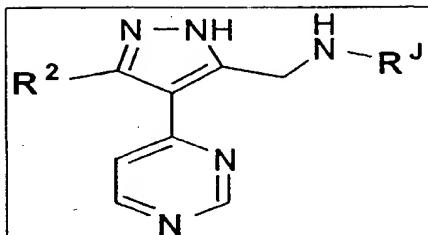
 R^2 R^4

B-2133					
B-2134					
B-2135					
B-2136					
B-2137					
B-2138					
B-2139					
B-2140					
B-2141					
B-2142					

Example#

 R^2 R^4

B-2143					
B-2144					
B-2145					
B-2146					
B-2147					
B-2148					
B-2149					

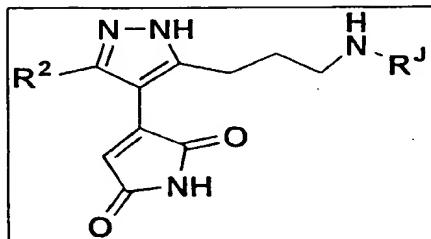


Examples B-2150 through B-2173 are prepared from Scaffold C-32

Example#	R ²	R ^j			
B-2150					
B-2151					
B-2152					
B-2153					
B-2154					
B-2155					
B-2156					

Example#	R ²	R ^J			
B-2157					
B-2158					
B-2159					
B-2160					
B-2161					
B-2162					
B-2163					
B-2164					
B-2165					
B-2166					

Example#	R ²	R ³			
B-2167					
B-2168					
B-2169					
B-2170					
B-2171					
B-2172					
B-2173					

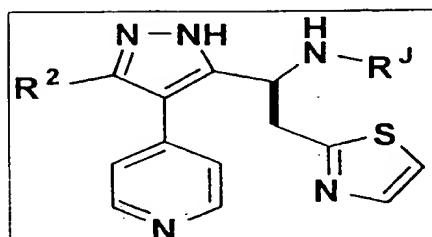


Examples 2174 through B-2197 are prepared from Scaffold C-64

Example#	R ²	R ^J			
B-2174					
B-2175					
B-2176					
B-2177					
B-2178					
B-2179					
B-2180					

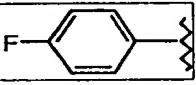
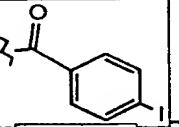
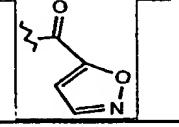
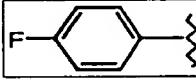
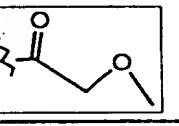
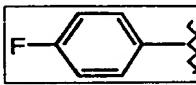
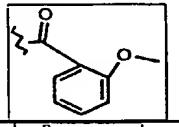
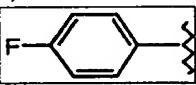
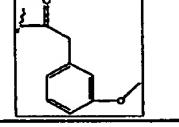
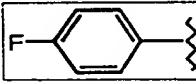
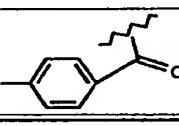
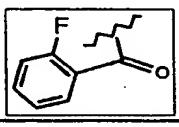
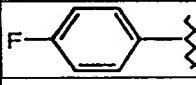
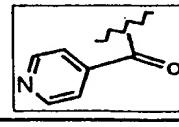
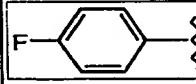
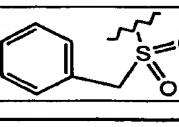
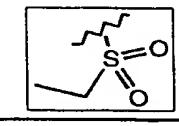
Example#	R ²	R ⁴			
B-2181					
B-2182					
B-2183					
B-2184					
B-2185					
B-2186					
B-2187					
B-2188					
B-2189					
B-2190					

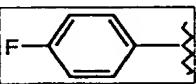
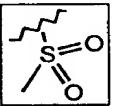
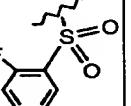
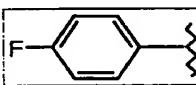
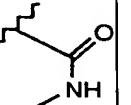
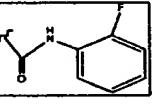
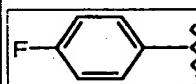
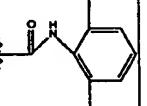
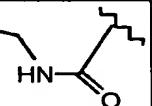
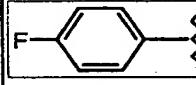
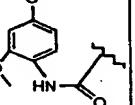
Example#	R ²	R ^J			
B-2191					
B-2192					
B-2193					
B-2194					
B-2195					
B-2196					
B-2197					

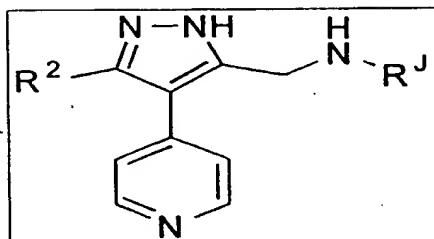


Examples B-2198 through B-2221 re prepared from Scaffold C-22

Example#	R ²	R ^j			
B-2198					
B-2199					
B-2200					
B-2201					
B-2202					
B-2203					
B-2204					

Example#	R ²	R ^J			
B-2205					
B-2206					
B-2207					
B-2208					
B-2209					
B-2210					
B-2211					
B-2212					
B-2213					
B-2214					

Example#	R ²	R ^J			
B-2215					
B-2216					
B-2217					
B-2218					
B-2219					
B-2220					
B-2221					

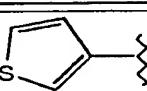
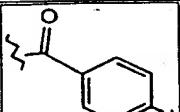
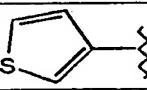
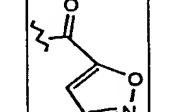
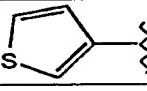
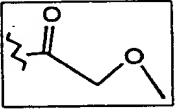
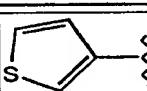
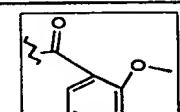
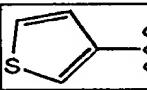
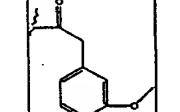
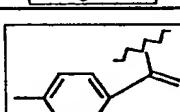
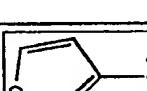
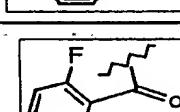
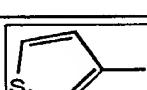


Examples B-2222 through B-2245 are prepared from Scaffold C-29

Example#	R^2	R^J			
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B-2223					
B-2224					
B-2225					
B-2226					
B-2227					
B-2228					

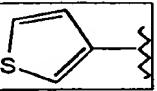
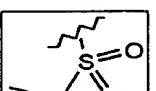
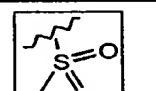
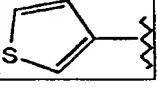
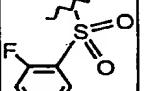
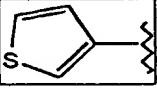
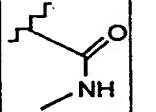
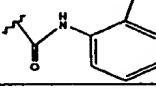
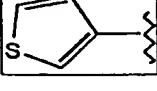
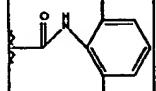
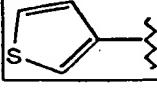
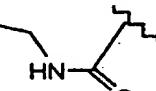
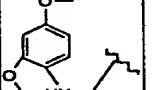
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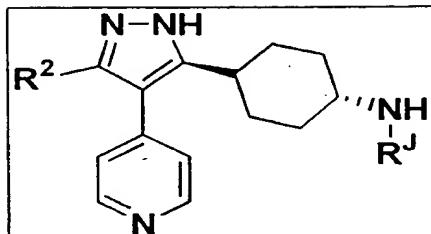
 R^2 R^J

B-2229					
B-2230					
B-2231					
B-2232					
B-2233					
B-2234					
B-2235					
B-2236					
B-2237					

Example#

 R^2 R^J

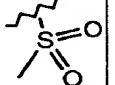
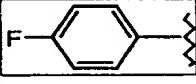
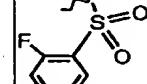
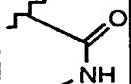
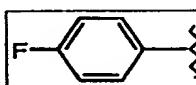
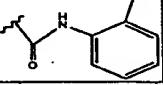
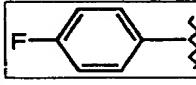
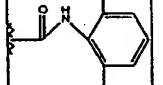
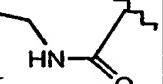
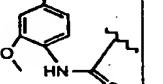
B-2238					
B-2239					
B-2240					
B-2241					
B-2242					
B-2243					
B-2244					
B-2245					



Examples B-2246 through B-2269 are prepared from Scaffold C-35

Example#	R ²	R ^J			
B-2246					
B-2247					
B-2248					
B-2249					
B-2250					
B-2251					
B-2252					

Example#	R ²	R ⁴			
B-2253					
B-2254					
B-2255					
B-2256					
B-2257					
B-2258					
B-2259					
B-2260					
B-2261					
B-2262					

Example#	R ²	R ⁴			
B-2263					
B-2264					
B-2265					
B-2266					
B-2267					
B-2268					
B-2269					

SUBSTITUTE SHEET (RULE 28)

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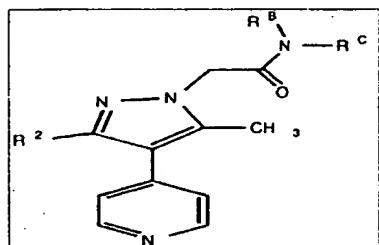
10

Examples B-2270 through B-2317

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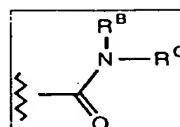
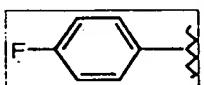
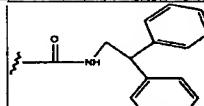
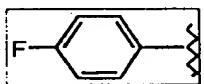
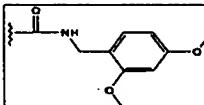
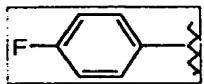
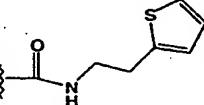
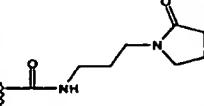
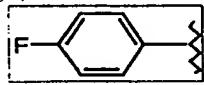
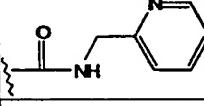
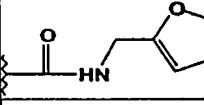
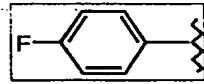
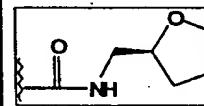
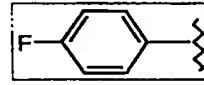
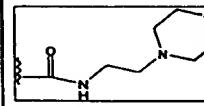
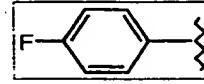
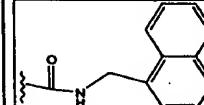
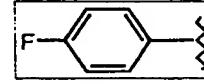
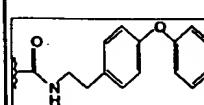
In a parallel array reaction block containing 48 fritted vessels, each reaction vessel was charged with 250 mg of polymer bound carbodiimide **B48** (1.0 mmol/g resin) and a solution of the acid-containing scaffold **C-49** in dimethylformamide (0.1 M, 500 uL). To each slurry was added a solution of pyridine in dichloromethane (0.2 M, 1000 uL) followed by a solution of a unique amine **B47** (0.2 M, 375 uL) in dimethylformamide. The reaction mixtures were agitated on a Labline benchtop orbital shaker at 250 RPM for 16-20 h at ambient temperature. The reaction mixtures were filtered into conical vials and the polymer was washed with 1.5 mL of dimethylformamide and 2.0 mL of dichloromethane. The filtrates were evaporated to dryness in a Savant apparatus and dimethylformamide (350 uL) was added to each conical vial to dissolve the residue. A solution of tetrafluorophthalic anhydride (1.0 M, 150 uL) in

dimethylformamide was added to the reconstituted conical vials and the mixture incubated for 2 hours at ambient temperature. Polyamine polymer **B33** (4.0 meq N/g resin, 250 mg) and 1.0 mL dichloromethane was then added to the reaction mixture in each conical vial. After agitating the reaction mixtures for 16 h at 250 RPM on an orbital shaker at ambient temperature, the mixtures were filtered through a polypropylene syringe tube fitted with a porous frit. The polymers were washed twice with dimethylformamide (1.0 mL each) and the filtrates and washings collected in conical vials. The filtrates were evaporated to dryness and weighed to afford the desired amide products **B-2270 through B-2317** as oils or solids. The analytical data and yields for the products prepared in this manner are listed below.



	R^2	Structure of the N-(Rc)Acyl group	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2270			12	352	353
B-2271			39	432	433
B-2272			26	400	-
B-2273			14	396	397
B-2274			30	434	435
B-2275			43	443	-
B-2276			35	364	365

616

	R^2	 	Yield	Calcd. Mass Spec.	Observed Mass Spec
				M	$M+H$
B-2277			33	490	-
B-2278			53	460	461
B-2279			10	420	-
B-2280			7	435	436
B-2281			18	401	402
B-2282			22	390	413 ^a *M+Na
B-2283			10	394	417 ^a *M+Na
B-2284			7	423	-
B-2285			23	450	-
B-2286			4	506	-

617

	R^2	Chemical Structure of Product	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2287			5	437	438
B-2288			8	435	436
B-2289			4	450	451
B-2290			9	456	457
B-2291			9	415	416
B-2292			5	368	369
B-2293			5	366	367
B-2294			5	381	382
B-2295			16	410	411
B-2296			4	483	-

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H+
B-2297			7	490	-
B-2298			4	537	-
B-2299			4	507	508
B-2300			7	442	-
B-2301			20	396	397
B-2302			30	459	-
B-2303			6	482	-
B-2304			5	395	396
B-2305			10	460	-
B-2306			11	466	467

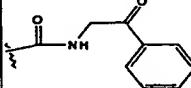
619

	R^2	Chemical Structure	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2307			5	421	422
B-2308			26	470	-
B-2309			24	424	425
B-2310			9	348	-
B-2311			21	338	339
B-2312			28	398	399
B-2313			6	410	-
B-2314			15	363	364
B-2315			11	444	-
B-2316			11	418	-

WO 98/52940

PCT/US98/10436

620

R ²	Chemical Structure	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H	
B-2317			36	428	-

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By analogy to the procedure identified above for the preparation of Examples B-2270 through B-2317, the following examples B-2318 through B-2461 were prepared.

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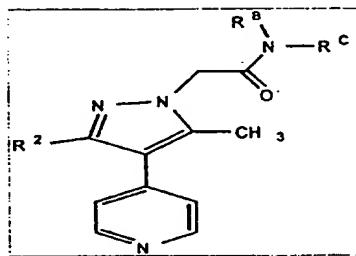
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30

SUBSTITUTE SHEET (RULE 26)

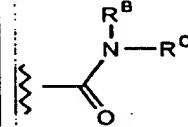
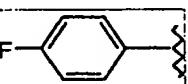
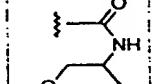
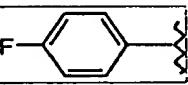
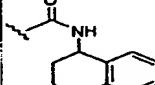
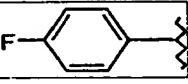
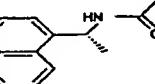
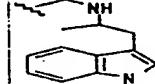
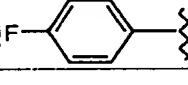
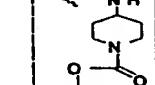
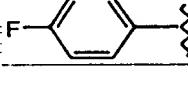
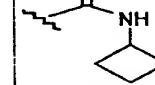
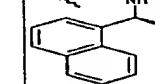
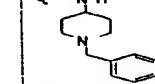
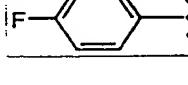
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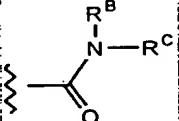
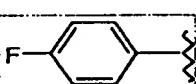
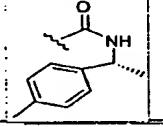
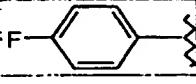
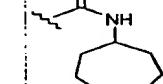
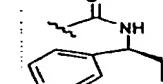
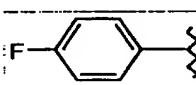
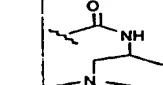
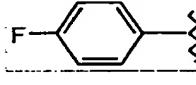
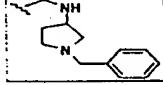
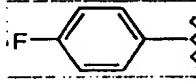
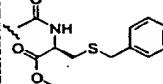
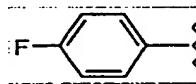
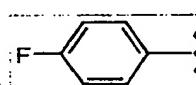
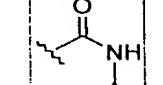
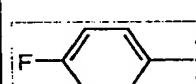
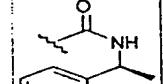
	R^2	R^{B} N---R^{C}	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2318			23	426	427
B-2319			23	394	-
B-2320			50	490	491
B-2321			49	426	427
B-2322			40	366	367
B-2323			68	410	411
B-2324			57	456	457

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	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2325			41	382	383
B-2326			71	440	441
B-2327			36	464	465
B-2328			32	467	468
B-2329			34	465	466
B-2330			26	364	365
B-2331			38	464	465
B-2332			33	483	484
B-2333			36	378	379

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	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2334			44	428	429
B-2335			27	406	407
B-2336			41	428	429
B-2337			27	423	424
B-2338			33	469	470
B-2339			52	518	519
B-2340			64	442	443
B-2341			41	350	351
B-2342			34	414	415

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2343			29	424	425
B-2344			33	492	493
B-2345			30	420	421
B-2346			35	474	475
B-2347			34	392	393
B-2348			51	458	459
B-2349			73	517	518
B-2350			22	448	449
B-2351			64	486	487

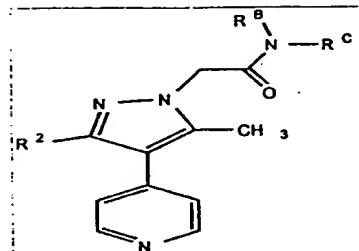
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B-2352			41	482	483
B-2353			57	438	439
B-2354			63	484	485
B-2355			28	536	537
B-2356			29	408	409
B-2357			41	436	437
B-2358			41	451	452
B-2359			57	502	503
B-2360			46	496	497

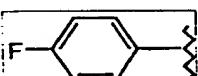
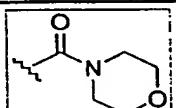
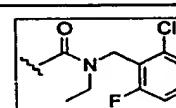
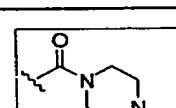
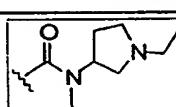
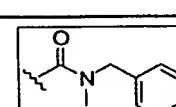
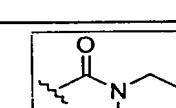
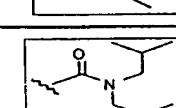
627

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2361			13	476	477
B-2362			46	493	494
B-2363			57	396	397
B-2364			61	438	439
B-2365			72	424	425

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	R^2	Structure of Compound	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2366			34	380	381
B-2367			52	480	481
B-2368			35	407	407
B-2369			31	435	436
B-2370			33	414	415
B-2371			28	366	367
B-2372			37	422	423

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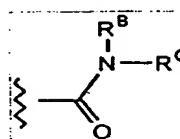
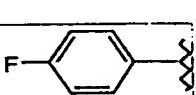
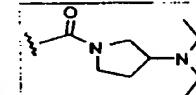
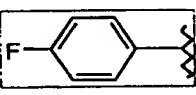
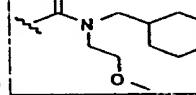
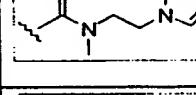
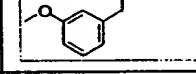
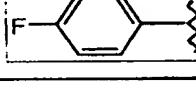
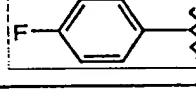
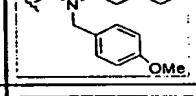
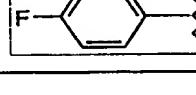
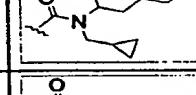
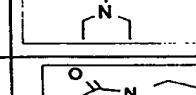
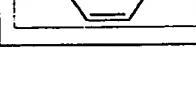
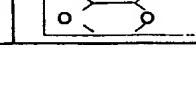
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	R^2	Chemical Structure of General Compound	Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2373			50	432	433
B-2374			29	382	383
B-2375			35	395	396
B-2376			36	428	429
B-2377			68	438	439
B-2378			55	446	447
B-2379			33	364	365
B-2380			51	421	422
B-2381			52	429	430

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			Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2382			48	407	408
B-2383			53	382	383
B-2384			38	447	448
B-2385			59	498	450
B-2386			45	429	430
B-2387			74	558	-
B-2388			53	475	-
B-2389			33	493	494
B-2390			53	487	488

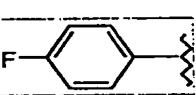
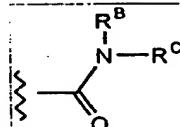
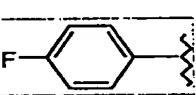
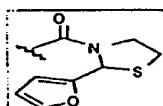
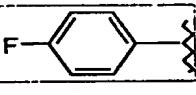
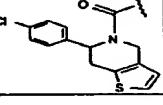
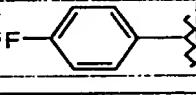
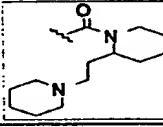
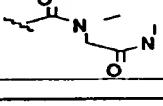
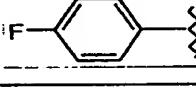
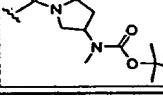
631

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2391			30	435	436
B-2392			57	464	465
B-2393			50	418	419
B-2394			65	488	489
B-2395			59	437	438
B-2396			34	534	535
B-2397			32	516	517
B-2398			81	533	534
B-2399			55	502	-

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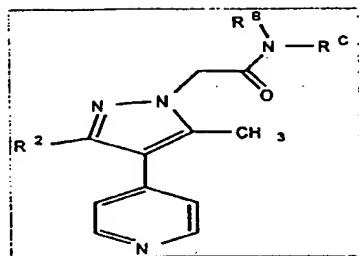
	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2400			34	381	382
B-2401			32	378	379
B-2402			71	519	520
B-2403			68	527	528
B-2404			62	447	448
B-2405			71	536	537
B-2406			47	394	395
B-2407			65	508	509
B-2408			34	495	496

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			Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2409			47	448	449
B-2410			73	542	543
B-2411			81	489	490
B-2412			54	409	410
B-2413			37	493	494

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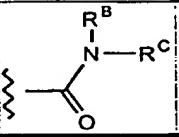
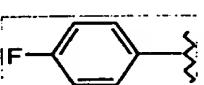
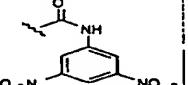
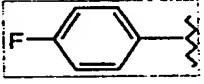
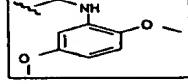
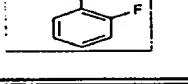
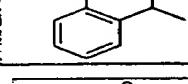
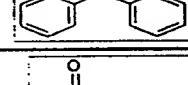
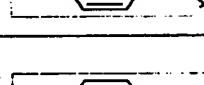
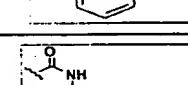
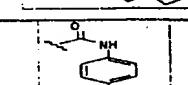
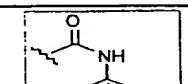
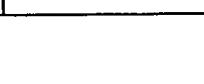


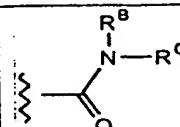
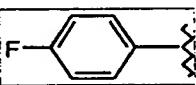
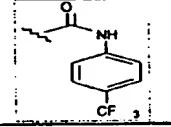
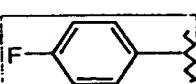
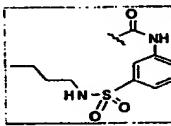
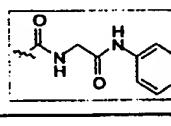
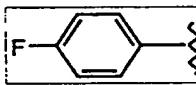
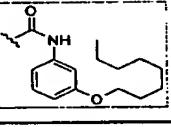
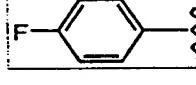
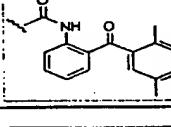
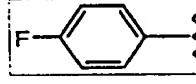
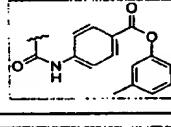
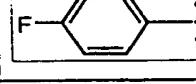
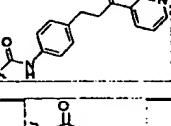
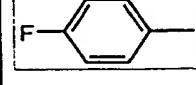
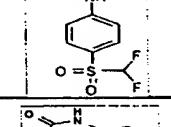
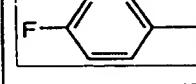
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B-2414			14	473	474
B-2415			19	421	422
B-2416			13	386	387
B-2417			29	414	415
B-2418			6	420	421
B-2419			10	454	-
B-2420			5	442	443

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	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2421			28	454	455
B-2422			47	420	421
B-2423			53	400	401
B-2424			15	400	401
B-2425			18	522	523
B-2426			38	464	465
B-2427			26	468	469
B-2428			22	432	433
B-2429			41	404	405

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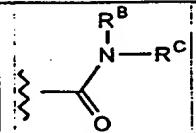
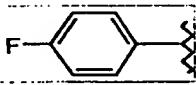
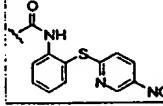
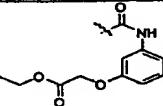
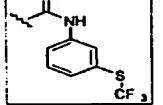
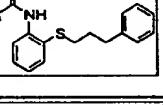
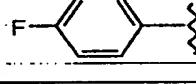
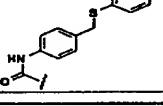
	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2430			15	476	477
B-2431			6	446	447
B-2432			37	404	405
B-2433			8	428	429
B-2434			13	476	477
B-2435			23	442	443
B-2436			5	486	487
B-2437			4	492	493
B-2438			58	422	423

	R ²		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2439			12	454	455
B-2440			8	521	522
B-2441			6	443	444
B-2442			37	514	515
B-2443			15	518	-
B-2444			52	520	-
B-2445			33	517	518
B-2446			70	500	501
B-2447			56	488	489

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	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2448			51	522	523
B-2449			19	512	513
B-2450			16	538	539
B-2451			71	511	512
B-2452			71	500	501
B-2453			61	470	-
B-2454			15	472	473
B-2455			39	520	-
B-2456			51	533	534

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	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2457			55	540	-
B-2458			22	488	489
B-2459			8	486	487
B-2460			13	534	535
B-2461			13	542	-

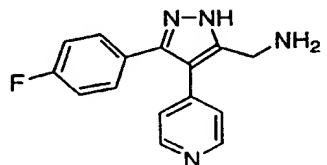
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Example C-1

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5-AMINOMETHYL-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE

20 **1-(4-fluorophenyl)-2-(4-pyridyl)-1-ethanone.** 4-
picoline (40 g, 0.43 mol) was added to a LiHMDS solution
(0.45 mol, 450 mL of a 1.0 M solution in THF) over 30
minutes at room temperature (a slight exotherm was
observed) The resulting solution was stirred for 1 h.
25 This solution was added to ethyl 4-fluorobenzoate (75.8
g, 0.45 mol, neat) over 1 h. The mixture was stirred
overnight (16 h). Water (200 mL) was added and the
mixture was extracted with EtOAc (2x200 mL). The organic
layer was washed with brine (1x200 mL) and dried over

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Na₂SO₄. The organic layer was filtered and the solvent was removed to leave oily solid. Hexane was added to the oil and the resulting solid was filtered and washed with hexane (cold). A yellow solid was isolated (50 g, 54%):
5 ¹H NMR (CDCl₃) δ 8.58 (d, J = 5.7 Hz, 2H), 8.02 (dd, J = 5.5, 8.0, 2H), 7.12-7.21 (m, 4H), 4.23 (s, 2H); ¹⁹F NMR (CDCl₃) δ -104.38 (m); LC/MS, t_r = 2.14 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 216; High Resolution MS Calcd for
10 C₂₃H₂₀N₄O₂F (M+H): 216.0825. Found: 216.0830 (Δ mmu = 0.5).

N-benzyloxycarbonyl-5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. A 3L round bottom flask fitted with a mechanical stirrer, N₂ inlet and an addition funnel was charged with 557 mL (0.56 mol) of 1 M t-BuOK in THF and 53 mL (0.56 mol) of t-BuOH. The ketone, 1 (60 g, 0.28 mol) was dissolved in 600 mL of THF and added to the stirred mixture at room temperature. A yellow precipitate formed and the mixture was stirred for 1 h. N-benzyloxycarbonyl-glycyl N-hydroxysuccinimide (128.6 g, 0.42 mol) was dissolved in 600 mL of THF and added dropwise at r.t. over 1h. The mixture was stirred for another 5 minutes and 150 mL of water was added. the pH 25 was adjusted to 6.7 with 70 mL of AcOH. Hydrazine monohydrate (41 mL in 100 mL of water) was added via an addition funnel. The mixture was stirred for 1 h and was diluted with 500 mL of water and 500 mL of ethyl acetate. The biphasic mixture was transferred to a sep funnel and the layers were separated. The aqueous layer was extracted with EtOAc (3x300 mL). The organic layer was

dried (Na_2SO_4), filtered and evaporated to leave 157 g of a crude reddish oil.

The oil was suspended in CH_2Cl_2 and filtered to remove any insoluble material (DCU, hydrazone of the monoketone). The solution was split into two portions and each portion was chromatographed (Biotage 75L, 3% EtOH/ CH_2Cl_2 then 6% EtOH/ CH_2Cl_2). The appropriate fractions were concentrated (some contamination from the monoketone and the hydrazone) from each portion to leave a yellow solid. The solid was suspended in ethyl acetate and heated to boiling for 10 minutes. The solution was allowed to cool to R.T. overnight. The precipitate was filtered to give 30 g of a white solid (27% yield of 2):
 ^1H NMR (DMF-d₇) δ 13.36 (s, 1H), 8.57 (d, J = 5.8 Hz, 2H), 7.16-7.52 (m, 11H), 5.11 (s, 2H), 4.48 (d, J = 5.4 Hz, 2H); ^{19}F NMR (DMF-d₇) δ -114.9 (m), -116.8 (m) (split fluorine signal is due to the pyrazole tautomers); LC/MS, t_r = 3.52 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 403; High Resolution MS Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{F}$ (M+H): 403.1570. Found: 403.1581 (Δ mmu = 1.1).

5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl)pyrazole. To a 1L Parr bottle was added 7 g (17.4 mmol) of 2 and 180 mL of MeOH and 90 mL of THF to give a clear solution. The bottle was purged with nitrogen and 1.5 g of 10% Pd/C (wet Degussa type E101) was added. The Parr bottle was pressured to 40 psi (H_2) and was agitated. Hydrogen uptake was 5 psi after 5 h. The bottle was repressured to 42 psi and was agitated overnight. The bottle was purged with N₂ and was filtered through Celite. The Celite was washed with MeOH (3x50 mL) and

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the filtrate was concentrated to give 4.5 g of an off-white solid (94%). ^1H NMR (DMSO-d₆) δ 8.52 (d, J = 4.63 Hz, 2H), 7.36 (dd, J = 5.64, 8.1 Hz, 2H), 7.16-7.30 (m, 4H), 3.79 (s, 2H); ^{19}F NMR (DMSO-d₆) δ -114.56 (m); LC/MS, 5 t_r = 1.21 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min., at 254 nm at 50°C), M+H = 269 m/z; High Resolution MS Calcd for C₁₅H₁₄N₄F (M+H): 269.1202. Found: 269.1229 (Δ mmu = 2.7).

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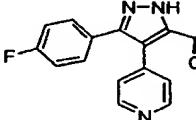
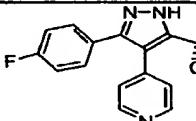
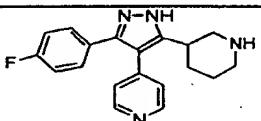
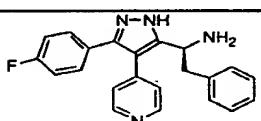
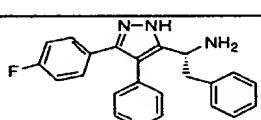
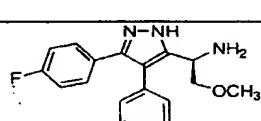
The following pyridylpyrazoles (C-2 through C-21, Table C-1) were prepared according to the experimental procedure described above for example C-1.

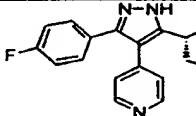
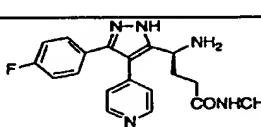
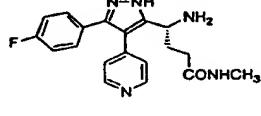
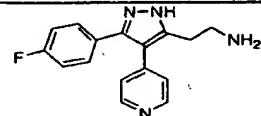
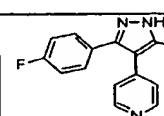
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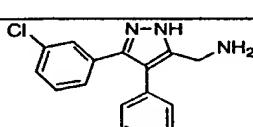
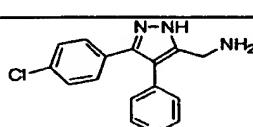
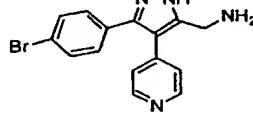
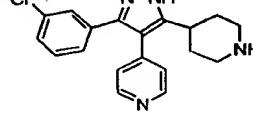
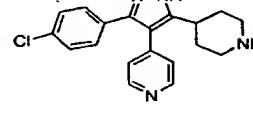
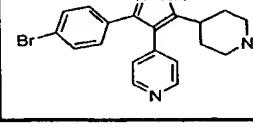
Table C-1.

Example No.	Structure	MW, M + H Calculated Found	^1H NMR (solvent), ppm
C-2		323.1672 323.1670	(DMF-d ₇): 8.77 (t, J = 4.4 Hz, 2H), 7.60 (m, 2H), 7.44 (t, J = 4.4 Hz, 2H), 7.35 (m, 2H), 3.22 (bd, 2H), 3.01 (septet, J = 5.3 Hz, 1H), 2.74 (m, 2H), 1.95 (m, 4H)

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C-3		282.127 (M) 282.1245 (M, EI)	(DMF-d ₇): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.34 (m, 2H), 4.40-4.37 (m, 1H), 1.56 (br s, 3H)
C-4		282.127 (M) 282.1147 (M, EI)	(DMF-d ₇): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.35 (m, 2H), 4.40-4.37 (m, 1H), 1.57 (br s, 3H)
C-5		323.1672 323.1687	(DMSO-d ₆): 8.56 (br, 2H), 7.32 (m, 2H), 7.18 (m, 4H), 2.91 (m, 2H), 2.71 (m, 2H) 1.88 (m, 1H), 1.65 (m, 2H), 1.40 (m, 2H)
C-6		359 359	(DMSO-d ₆): 8.46 (d, J = 4.6 Hz, 2H), 7.32-7.13 (m, 7H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.95 (m, 2H)
C-7		359 359	(DMSO-d ₆): 8.46 (d, J = 5.4 Hz, 2H), 7.32-7.28 (m, 2H), 7.20-7.12 (m, 5H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.94 (m, 2H)
C-8		313.1465 313.1492	(DMSO-d ₆): 13.83 (bs, 1H), 8.61 (d, J = 5.7 Hz, 2H), 8.33 (bs, 1H), 7.33 (m, 6H), 4.44 (m, 1H), 3.63 (m, 2H), 3.27 (s, 3H)

C-9		313.1465 313.1457	(DMSO-d ₆): 8.55 (dd, J = 1.5, 4.4 Hz, 2H), 7.37-7.32 (m, 2H), 7.26 (dd, J = 1.6, 4.4 Hz, 2H), 7.22-7.16 (m, 2H), 4.06 (t, J = 6.5 Hz, 1H), 3.49 (d, J = 6.6 Hz, 2H), 3.20 (s, 3H)
C-10		354 354	(DMSO-d ₆): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-11		354 354	(DMSO-d ₆): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-12		283.1359 283.1363	(DMSO-d ₆): 8.53 (d, J = 5.0 Hz, 2H), 7.37-7.32 (m, 2H), 7.21-7.17 (m, 4H), 2.83 (d, J = 6.0 Hz, 2H), 2.77 (d, J = 6.0 Hz, 2H)
C-13		297.1515 297.1515	(DMSO-d ₆): 8.53 (d, J = 5.4 Hz, 2H), 7.34 (dd, J = 5.8, 8.2 Hz, 2H), 7.18

			(dd, J = 5.8, 9.8 Hz, 4H), 2.68 (t, J = 7.3 Hz, 2H), 2.52 (m, 2H), 1.64 (m, 2H)
C-14		284.0829 284.0806	(CD ₃ OD) : 8.74 (br, 2H), 7.77 (br, 2H), 7.45-7.58 (m, 3H), 7.30-7.40 (m, 1H), 4.43 (s, 2H)
C-15		285 285	(DMSO-d ₆) : 8.53 (br, 2H), 7.56 (br, 2H), 7.26 (m, 4H), 3.75 (br, 2H)
C-16		329, 331 329, 331	(DMSO-d ₆) : 8.53 (d, J = 4.4 Hz, 2H), 7.42 (d, J = 7.9 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 4.6 Hz, 2H), 3.76 (bs, 2H)
C-17		339 339	(DMSO-d ₆) : 8.53 (t, J = 4.3 Hz, 2H), 7.33 (m, 3H), 7.19 (t, J = 4.6 Hz, 2H), 7.14 (d, J = 7.3 Hz, 1H), 3.23 (m, 2H), 2.88, (m, 3H), 1.92, (m, 3H), 1.70 (m, 1H)
C-18		339	(DMSO-d ₆) : 8.57 (d, J = 4.6 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 4.8 Hz, 2H), 3.18 (bd, 2H), 2.88 (m, 1H), 2.76 (m, 2H), 1.82 (br, 4H)
C-19		383, 385 383, 385	(DMSO-d ₆) : 8.56 (br, 2H), 7.52 (br, 2H), 7.14-7.29 (m, 4H), 2.99 (br, 2H),

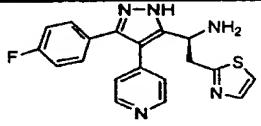
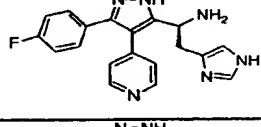
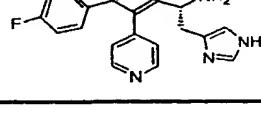
			2.71 (br, 1H), 2.51 (br, 2H), 1.68 (br, 4H)
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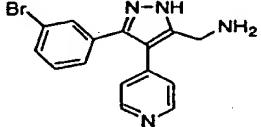
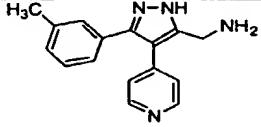
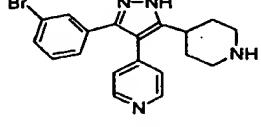
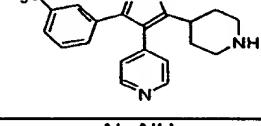
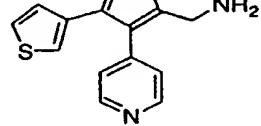
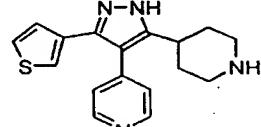
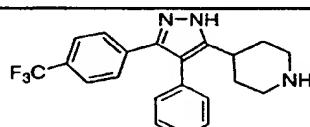
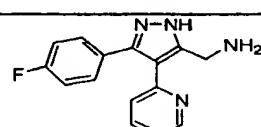
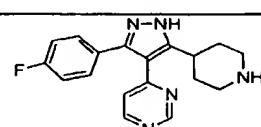
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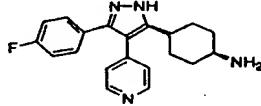
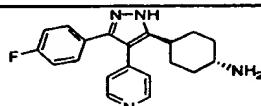
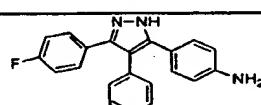
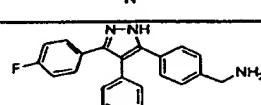
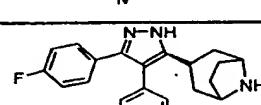
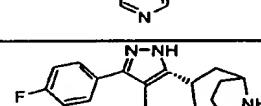
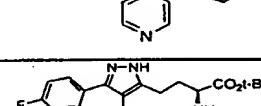
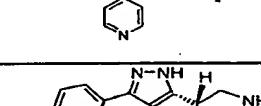
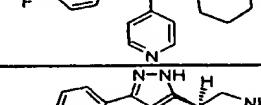
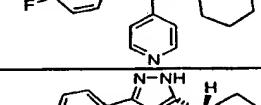
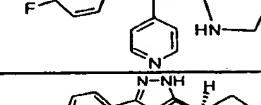
The following pyridylpyrazoles (C-22 through C-40, Table C-2) are prepared utilizing the general schemes C-1 and C-2 and the experimental procedure described for example 15 C-1 above.

Table C-2

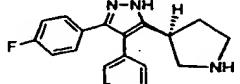
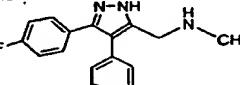
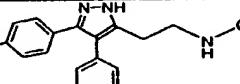
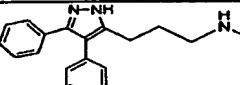
Cmpd. No.	Structure
C-22	
C-23	
C-24	

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C-25	
C-26	
C-27	
C-28	
C-29	
C-30	
C-31	
C-32	
C-33	

C-34	
C-35	
C-36	
C-37	
C-38	
C-39	
C-40	
C-41	
C-42	
C-43	
C-44	

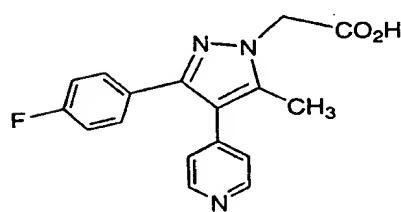
650

C-45	
C-46	
C-47	
C-48	

5

Example C-49

10



15

Step A

The pyrazole (2.60 g, 10.3 mmol) from example 4 was suspended in 52 mL of dichloroethane and 52 mL of 2.5 M

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NaOH. Tetrabutylammonium hydroxide (0.5 mL of a 1 M aqueous solution) was added to the stirred mixture. To this mixture was added t-butyl bromoacetate (2.10 g, 10.8 mmol). The reaction mixture was stirred at room temperature for 4 h. The mixture was poured onto 200 mL of CH₂Cl₂ and 200 mL of H₂O. The phases were separated and the organic phase was washed with water (1x100 mL) and brine (1x100 mL). The organic layer was dried over Na₂SO₄ and was filtered. The solvent was removed to leave an off-white solid. This solid was triturated with hexane and the resulting solid isolated by filtration. The solid was washed with hexane to leave 3.4 g of a white solid (90%).

15

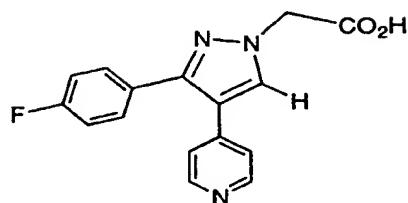
Step B

The alkylated pyrazole (3.7 g, 10.1 mmol) from Step A was treated with 57 mL of 4 N HCl in dioxane. The solution was stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was dissolved in THF. The solution was treated with propylene oxide (10.3 mmol) and was stirred for 1 h at room temperature. The solvent was removed to leave an oil. The residual solvent was chased with several portions of EtOH. The resulting solid was triturated with Et₂O and the title compound Example C-49 was isolated by filtration to afford 3.0 g of an off-white solid (95%). Mass spec: M+H cald: 312; found 312. ¹H NMR (DMSO-d₆): 8.81 (d, J = 6.4 Hz, 2H), 7.73 (d, J =

652

5.8 Hz, 2H), 7.40 (m, 2H), 7.23 (t, J = 8.5 Hz, 1H), 5.16 (s, 2H), 2.40 (s, 3H).

5

Example C-50

According to the procedure described above in Example C-49, Example C-50 was also prepared starting from 4-[3-(4-fluorophenyl)-1H-pyrazole-4-yl]pyridine. Mass spec: M+H cald: 298; found 298. ^1H NMR (DMSO-d6): 8.75 (d, J = 6.4 Hz, 2H), 8.68 (s, 1H), 7.78 (d, J = 6.6 Hz, 2H), 7.52 (dd, J = 5.4, 8.5 Hz, 2H), 7.31 (t, J = 8.9 Hz, 2H), 5.16 (s, 2H).

Example C-51

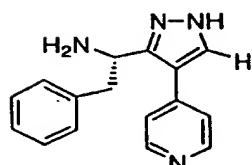
20



Starting with the N-Boc-piperidinyl analog of Example C-2, Example C-51 is also prepared according to the methods described in Scheme C-1.

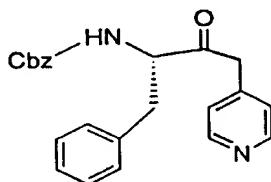
Example C-52

5



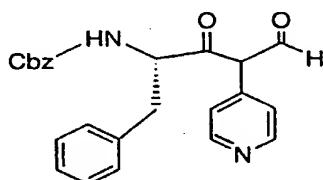
Step A: Picoline is treated with a base chosen from but not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH in an organic solvent such as THF, ether, t-BuOH or dioxane from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The picoline solution is then added to a solution of N-Cbz-(L)-phenylalaninyl N-hydroxysuccinimide. The reaction is allowed to stir from 30 minutes to 48 hours during which time the temperature may range from -20 °C to 120 °C. The mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the pyridyl monoketone is isolated as a crude solid which could be purified by crystallization and/or chromatography.

20



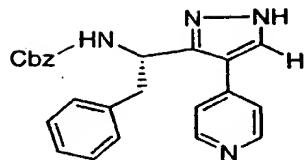
25 Step B: A solution of the pyridyl monoketone in ether, THF, tBuOH, or dioxane is added to a base chosen from but

not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH contained in hexane, THF, ether, dioxane, or tBuOH from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. Formyl acetic anhydride is then added as a solution in THF, ether, or dioxane to the monoketone anion while the temperature is maintained between -50 °C and 50 °C. The resulting mixture is allowed to stir at the specified temperature for a period of time from 5 minutes to several hours. The resulting pyridyl diketone intermediate is utilized without purification in Step C.



Step C: The solution containing the pyridyl diketone is quenched with water and the pH is adjusted to between 4 and 8 utilizing an inorganic or organic acid chosen from HOAc, H₂SO₄, HCl, or HNO₃. The temperature during this step is maintained between -20 °C and room temperature. Hydrazine or hydrazine hydrate is then added to the mixture while maintaining the temperature between -20 °C and 40 °C for a period of 30 minutes to several hours. The mixture is then poured into water and extracted with an organic solvent. The N-Cbz-protected pyridyl pyrazole is obtained as a crude solid which is purified by chromatography or crystallization.

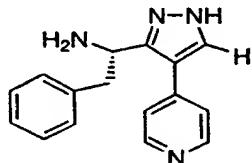
655



5 Step: D

The CBZ protecting group is cleaved using hydrogen gas under pressure and Pd-C in an alcohol solvent, affording scaffold C-52 after filtration and concentration.

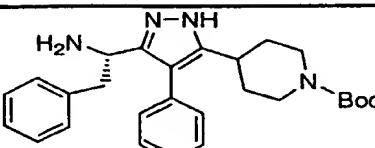
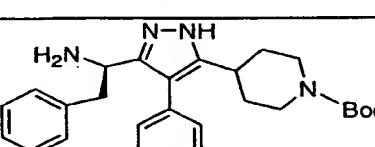
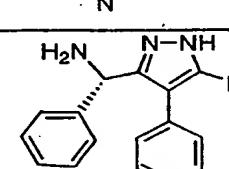
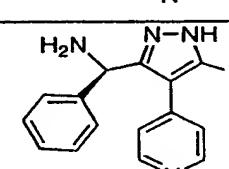
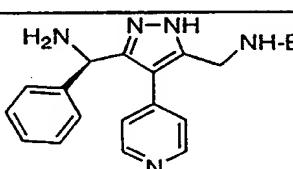
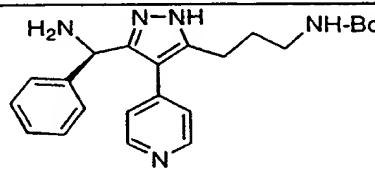
10



- 15 The following compounds C-53 through C-59 in Table C-3 are prepared according to the general procedure described above for the preparation of C-52.

Table C-3

Example No.	Structure
C-53	

C-54	
C-55	
C-56	
C-57	
C-58	
C-59	

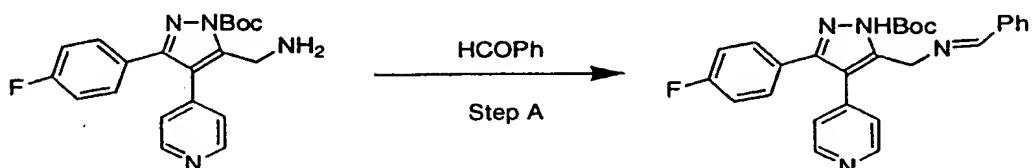
Example C-60

5 Step A:

A Boc protected pyridylpyrazole is treated with benzaldehyde in methylene chloride at room temperature in

the presence of a drying agent for a period of time ranging from 1-24 h. Solvent is then evaporated and the resulting imine is used in step B without further purification.

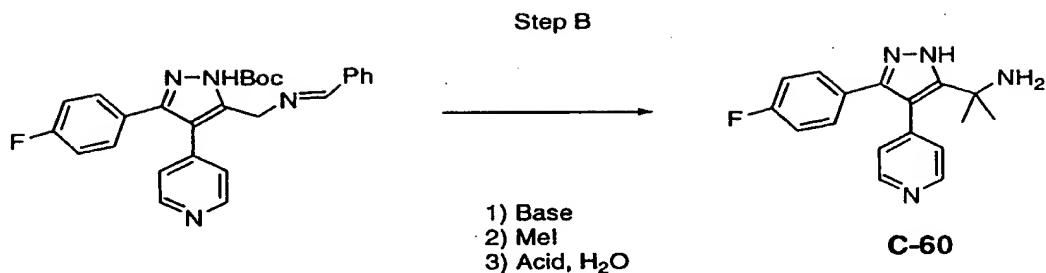
5



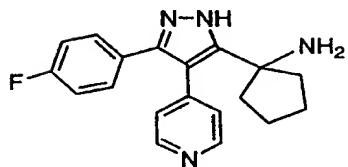
Step B:

The pyridylpyrazole imine is dissolved in THF and stirred under nitrogen at temperatures ranging from -78 to -20 °C. A base such as LDA, n-BuLi, or LiHMDS is added dropwise to the mixture which is then stirred for an additional 10 minutes to 3 h. Two equivalents of a methyl iodide are then added to the mixture and stirring is continued for several hours. The mixture is then quenched with acid and allowed to warm to room temperature and stirred several hours until cleavage of the Boc and the imine functions is complete. The pH is adjusted to 12 and then the mixture is extracted with an organic solvent, which is dried and evaporated. The crude pyridylpyrazole is then crystallized and/or chromatographed to give purified C-60.

658



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Example C-61

- 10 Example C-61 is prepared according to the method described in example C-60, substituting 1,4-dibromobutane for methyl iodide.

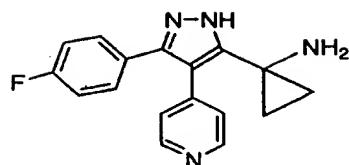
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Example C-62

20

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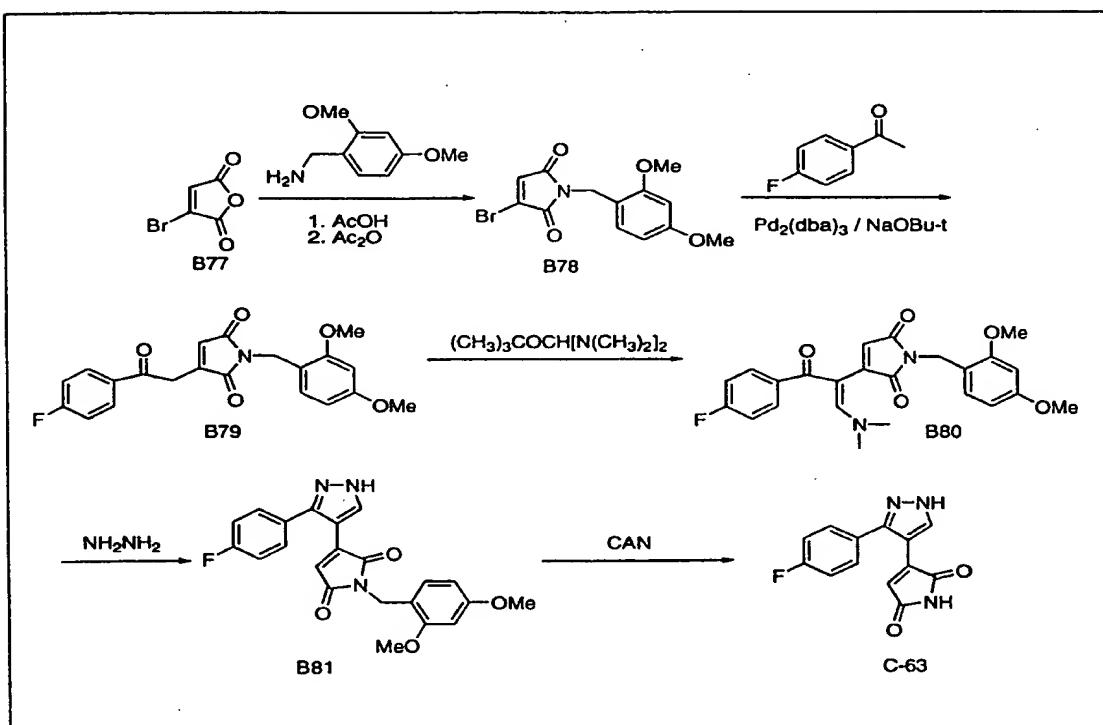


Example C-62 is prepared according to the method described in example C-60, substituting 1,3-dibromoethane for methyl iodide.

5

Example C-63

The synthesis of compound C-63 starts with the
10 condensation reaction of bromomaleic anhydride B77 with
2, 4-dimethoxybenzylamine in acetic acid and acetic
anhydride. The maleimide B78 is then treated with 4'-
fluoroacetophenone in the presence of catalytic amount
Pd₂(dba)₃ and sodium t-butoxide to form the
15 fluoroacetophenone substituted maleimide B79. B79 is
then treated with tert-butoxybis(dimethylamino)methane to
yield the α -ketoenamine B80. The α -ketoenamine B80 is
condensed with hydrazine to form the N-protected
maleimide pyrazole B81. The 2,4-dimethoxybenzyl group is
20 cleaved with ceric ammonium nitrate (CAN) to give the
title compound C-63.

**Example C-64**

5



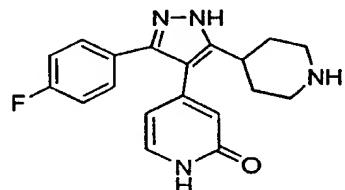
Using the method described in Schemes C-6 and C-7,
10 Example 64 is prepared.

Example C-65

5

Using the method described in Schemes C-6 and C-7,
Example 65 is prepared.

10

Example C-66

15

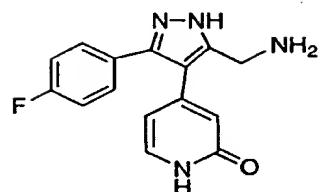
Using the method described in Schemes C-6 and C-7,
Example C-66 is synthesized, substituting N-2,4-
20 dimethoxybenzyl-4-bromopyridone for B78.

25

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Example C-67

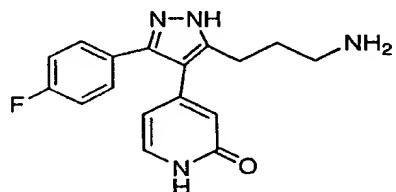
5



Using the method described in Schemes C-6 and C-7,
Example C-67 is synthesized, substituting N-2,4-
10 dimethoxybenzyl-4-bromopyridone for B78, and substituting
N-Boc-glycyl N-hydroxysuccinimide for B82.

Example C-68

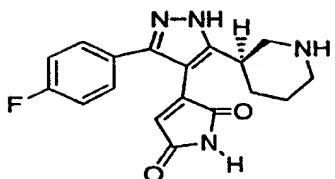
15



Using the method described in Schemes C-6 and C-7,
20 Example C-68 is synthesized, substituting N-2,4-
dimethoxybenzyl-4-bromopyridone for B78.

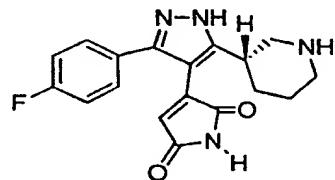
25

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Example C-69

Using the method described in Schemes C-6 and C-7, Example 69 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

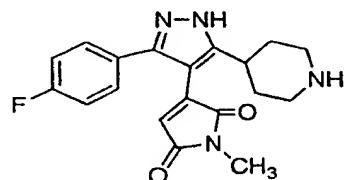
10

Example C-70

15 Using the method described in Schemes C-6 and C-7, Example 70 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

Example C-71

20

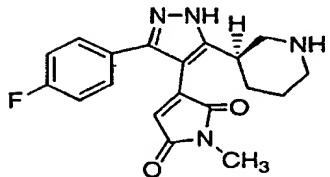


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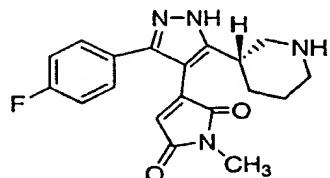
Using the method described in Schemes C-6 and C-7, Example 71 is prepared, substituting N-methyl-3-bromomaleimide for B78.

5

Example C-72

- 10 Using the method described in Schemes C-6 and C-7, Example 72 is prepared, substituting N-methyl-3-bromomaleimide for B78, and substituting N-Boc-nipecotyl N-hydroxysuccinimide for B83.

15

Example C-73

- 20 Using the method described in Schemes C-6 and C-7, Example 73 is prepared, substituting N-methyl-3-bromomaleimide for B78 and substituting N-Boc-nipecotyl N-hydroxysuccinimide for B83.

25

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Biological data from compounds of Examples B-0001 through B-1573 and of Examples B-2270 through B-2462 are shown in
5 the following tables.

In vitro P38-alpha kinase inhibitory data are shown in the column identified as:

"P38 alpha kinase IC₅₀, uM or % inhib @ conc. (uM)"

10

In vitro whole cell assay for measuring the ability of the compounds to inhibit TNF production in human U937 cells stimulated with LPS are shown in the column
15 identified as:

"U937 Cell IC₅₀, uM or % inhib @ conc., (uM)"

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the mouse is shown
20 in the column identified as:

"Mouse LPS Model, % TNF inhib @ dose @ predose time"

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time indicates the number of hours before LPS challenge when
25 the compound is administered.

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the rat is shown in the column identified as:

30 "Rat LPS Model, % TNF inhib @ dose @ predose time"

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time

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indicates the number of hours before LPS challenge when
the compound is administered.

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Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0001	53.0%@1.0uM	40.0% @1.0uM		
B-0002	71.0%@1.0uM	28.0%@10.0uM		
B-0003	70.0%@1.0uM	76.0% 10.0uM		
B-0004	80.0%@1.0uM	4.61uM		
B-0005	95.0%@1.0uM	2.97uM		
B-0006	82.0%@1.0uM	80%@10.0uM		
B-0007	74.0%@1.0uM	85.0%@10.0uM		
B-0008	42.0%@1.0uM	65.0%@10.0uM		
B-0009	0.04 uM	0.72uM		
B-0010	0.52 uM	0.65uM		
B-0011	0.03 uM	4.47uM		
B-0012	30.0%@1.0uM	44.0% @1.0uM		
B-0013	70.0%@1.0uM	84.0%@10.0uM		
B-0014	79.0%@1.0uM	80.0%@10.0uM		
B-0015	82.0%@1.0uM	80.0%@10.0uM		
B-0016	94.0%@1.0uM	3.98uM		
B-0017	56.0%@1.0uM	79.0%@10.0uM		
B-0018	60.0%@1.0uM	59.0%@10.0uM		
B-0019	84.0%@1.0uM	100.0%@10.0uM		
B-0020	73.0%@1.0uM	81.0%@10.0uM		
B-0021	68.0%@1.0uM	76.0%@10.0uM		
B-0022	69.0%@1.0uM	44.0@1.0uM		
B-0023	90.0%@1.0uM	77.0%@10.0uM		
B-0024	94.0%@1.0uM	52.0%@1.0uM		
B-0025	89.0%@1.0uM	79.0%@10.0uM		
B-0026	96.0%@1.0uM	3.27uM		
B-0027	94.0%@1.0uM	11.0uM		
B-0028	69.0%@1.0uM	45.0%@10.0uM		
B-0029	91.0%@1.0uM	58.0%@10.0uM		
B-0030	92.0%@1.0uM	75.0%@10.0uM		
B-0031	94.0%@1.0uM	100.0%@10.0uM		
B-0032	94.0%@1.0uM	78.0%@10.0uM		
B-0033	97.0%@1.0uM	10.0uM		
B-0034	95.0%@1.0uM	10.0uM		
B-0035	94.0%@1.0uM	10.0uM		
B-0036	92.0%@1.0uM	8.24uM		
B-0037	91.0%@1.0uM	86.0%@10.0uM		
B-0038	71.0%@1.0uM	84.0%@10.0uM		
B-0039	89.0%@1.0uM	72.0%@10.0uM		
B-0040	93.0%@1.0uM	2.3uM		
B-0041	65.0%@1.0uM	66.0%@10.0uM		
B-0042	94.0%@1.0uM	2.76uM		

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Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0043	0.22 uM	0.54uM		
B-0044	0.14 uM	0.19uM		
B-0045	94.0%@1.0uM	1.01uM		
B-0046	96.0%@1.0uM	54.0%@1.0uM		
B-0047	94.0%@1.0uM	74.0%@10.0uM		
B-0048	94.0%@1.0uM	76.0%@10.0uM		
B-0049	88%@1.0uM	33.0%@1.0uM		
B-0050	73%@1.0uM	34.0%@1.0uM		
B-0051	3.3uM	2.15uM	47%@100mpk@-6h	79%@3mpk@-4h
B-0052	92%@1.0uM	15.0%@1.0uM		
B-0053	95%@1.0uM	34.0%@1.0uM		
B-0054	90%@1.0uM	30.0%@1.0uM		
B-0055	93%@1.0uM	>1.0uM		
B-0056	96%@1.0uM	21.0%@1.0uM		
B-0057	96%@1.0uM	29.0%@1.0uM		
B-0058	79%@1.0uM	18.0%@1.0uM		
B-0059	83%@1.0uM	35.0%@1.0uM		
B-0060	73%@1.0uM	22.0%@1.0uM		
B-0061	62%@1.0uM	27.0%@1.0uM		
B-0062	94%@1.0uM	36.0%@1.0uM		
B-0063	96%@1.0uM	40.0%@1.0uM		
B-0064	90%@1.0uM	4.0%@1.0uM		
B-0065	83%@1.0uM	21.0%@1.0uM		
B-0066	94%@1.0uM	28.0%@1.0uM		
B-0067	91%@1.0uM	1.0%@1.0uM		
B-0068	72%@1.0uM	22.0%@1.0uM		
B-0069	96%@1.0uM	37.0%@1.0uM		
B-0070	92%@1.0uM	30.0%@1.0uM		
B-0071	86%@1.0uM	31.0%@1.0uM		
B-0072	77%@1.0uM	32.0%@1.0uM		
B-0073	91%@1.0uM	24.0%@1.0uM		
B-0074	92%@1.0uM	42.0%@1.0uM		
B-0075	91%@1.0uM	35.0%@1.0uM		
B-0076	58%@1.0uM	21.0%@1.0uM		
B-0077	0.8uM	10.0uM		
B-0078	80%@1.0uM	20.0%@1.0uM		
B-0079	93%@1.0uM	13.0%@1.0uM		
B-0080	73%@1.0uM	73.0%@1.0uM		
B-0081	92%@1.0uM	13.0%@1.0uM		
B-0082	47%@1.0uM	27.0%@1.0uM		
B-0083	0.22uM	6.51uM		
B-0084	56%@1.0uM	30.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0085	83%@1.0uM	21.0%@1.0uM		
B-0086	91%@1.0uM	37.0%@1.0uM		
B-0087	0.55uM	2.26uM	38%@30mpk@-6h	
B-0088	96%@1.0uM	9.0%@1.0uM		
B-0089	0.04uM	3.33uM		
B-0090	98%@1.0uM	52.0%@1.0uM		
B-0091	96%@1.0uM	40.0%@1.0uM		
B-0092	97%@1.0uM	34.0%@1.0uM		
B-0093	3.18 uM	1.25uM	30%@30mpk@-6h	
B-0094	96%@1.0uM	52.0%@1.0uM		
B-0095	98%@1.0uM	38.0%@1.0uM		
B-0096	91%@1.0uM	22.0%@1.0uM		
B-0097	72.0%@10.0uM	38.0%@1.0uM		
B-0098	66.0%@10.0uM	12.0%@1.0uM		
B-0099	43.0% @1.0uM	>1.0uM		
B-0100	75.0% @1.0uM	5.0uM		
B-0101	71.0% @1.0uM	2.11uM		
B-0102	81.0%@1.0uM	15.0%@1.0uM		
B-0103	71.0%@1.0uM	6.0%@1.0uM		
B-0104	56.0% @1.0uM	2.78uM		
B-0105	78.0%@1.0uM	5.0uM		
B-0106	62.0%@1.0uM	5.0uM		
B-0107	0.27uM	5.0uM		
B-0108	61.0%@1.0uM	4.85uM		
B-0109	45.0%@1.0uM	19.0%@1.0uM		
B-0110	66.0%@1.0uM	13.0%@1.0uM		
B-0111	57.0%@1.0uM	>1.0uM		
B-0112	97.0%@1.0uM	1.12uM		
B-0113	75.0%@1.0uM	43.0%@1.0uM		
B-0114	45.0%@1.0uM	3.92uM		
B-0115	47.0%@1.0uM	2.0%@1.0uM		
B-0116	73.0%@1.0uM	35.0%@1.0uM		
B-0117	0.46 uM	1.78 uM	30%@30mpk@-6h	
B-0118	1.18 uM	1.29 uM		
B-0119	89.0%@10.0uM	2.78uM		
B-0120	0.008 uM	0.21 uM	77%@100mpk@-6h	70%@3mpk@-4h
B-0121	79.0%@1.0uM	1.22uM		
B-0122	79.0%@10.0uM	2.0%@1.0uM		
B-0123	59.0%@1.0uM	>1.0uM		
B-0124	73.0%@1.0uM	15.0%@1.0uM		
B-0125	70.0%@10.0uM	17.0%@1.0uM		
B-0126	66.0%@1.0uM	1.57uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0127	82.0% @ 1.0uM	0.96uM		
B-0128	78.0% @ 1.0uM	1.81uM		
B-0129	51.0% @ 1.0uM	31.0% @ 1.0uM		
B-0130	69.0% @ 1.0uM	58.0% @ 1.0uM		
B-0131	43.0% @ 1.0uM	46.0% @ 1.0uM		
B-0132	76.0% @ 1.0uM	8.0% @ 1.0uM		
B-0133	51.0% @ 1.0uM	42.0% @ 1.0uM		
B-0134	60.0% @ 1.0uM	2.17uM		
B-0135	78.0% @ 1.0uM	58.0% @ 1.0uM		
B-0136	77.0% @ 1.0uM	44.0% @ 1.0uM		
B-0137	41.0% @ 1.0uM	37.0% @ 1.0uM		
B-0138	50.0% @ 1.0uM	32.0% @ 1.0uM		
B-0139	54.0% @ 10.0uM	17.0% @ 1.0uM		
B-0140	67% @ 10.0uM	9.0% @ 1.0uM		
B-0141	78.0% @ 1.0uM	10.0% @ 1.0uM		
B-0142	86.0% @ 1.0uM	12.0% @ 1.0uM		
B-0143	42.0% @ 1.0uM	3.63uM		
B-0144	86.0% @ 1.0uM	43.0% @ 1.0uM		
B-0145	54.0% @ 10.0uM	12.0% @ 1.0uM		
B-0146	77.0% @ 10.0uM	28.0% @ 1.0uM		
B-0147	44.0% @ 1.0uM	22.0% @ 1.0uM		
B-0148	51.0% @ 1.0uM	>1.0uM		
B-0149	1.15 uM	10.0 uM		
B-0150	27.0% @ 10.0uM	35.0% @ 1.0uM		
B-0151	43.0% @ 1.0uM	30.0% @ 1.0uM		
B-0152	51.0% @ 1.0uM	24.0% @ 1.0uM		
B-0153	57.0% @ 1.0uM	21.0% @ 1.0uM		
B-0154	65.0% @ 10.0uM	14.0% @ 1.0uM		
B-0155	40.0% @ 10.0uM	26.0% @ 1.0uM		
B-0156	42.0% @ 10.0uM	13.0% @ 1.0uM		
B-0157	48.0% @ 10.0uM	9.0% @ 1.0uM		
B-0158	58.0% @ 10.0uM	39.0% @ 1.0uM		
B-0159	54.0% @ 10.0uM	5.0% @ 1.0uM		
B-0160	59.0% @ 10.0uM	26.0% @ 1.0uM		
B-0161	72.0% @ 10.0uM	13.0% @ 1.0uM		
B-0162	23% @ 1.0uM	2.05 uM		
B-0163	20.0% @ 10.0uM	10.0% @ 1.0uM		
B-0164	37.0% @ 10.0uM	20.0% @ 1.0uM		
B-0165	70.0% @ 10.0uM	19.0% @ 1.0uM		
B-0166	45.0% @ 10.0uM	37.0% @ 1.0uM		
B-0167	40.0% @ 1.0uM	37.0% @ 1.0uM		
B-0168	44% @ 1.0uM	2.36 uM		

SUBSTITUTE SHEET (RULE 28)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0169	43.0% @1.0uM	21.0% @1.0uM		
B-0170	43.0% @1.0uM	30.0% @1.0uM		
B-0171	61.0% @10.0uM	21.0% @1.0uM		
B-0172	16.0% @10.0uM	11.0% @1.0uM		
B-0173	33.0% @10.0uM	48.0% @1.0uM		
B-0174	54.0% @10.0uM	43.0% @1.0uM		
B-0175	41.0% @10.0uM	31.0% @1.0uM		
B-0176	50.0% @1.0uM	30.0% @1.0uM		
B-0177	70.0% @10.0uM	27.0% @1.0uM		
B-0178	12.0% @10.0uM	35.0% @1.0uM		
B-0179	27.0% @10.0uM	37.0% @1.0uM		
B-0180	34.0% @10.0uM	23.0% @1.0uM		
B-0181	5.0%@1.0uM	2.0% @1.0uM		
B-0182	39.0% @10.0uM	40.0% @1.0uM		
B-0183	12.0% @10.0uM	34.0% @1.0uM		
B-0184	66.0% @10.0uM	17.0% @1.0uM		
B-0185	65.0% @10.0uM	25.0% @1.0uM		
B-0186	40.0% @1.0uM	25.0% @1.0uM		
B-0187	4.0% @10.0uM	14.0% @1.0uM		
B-0188	70.0% @10.0uM	35.0% @1.0uM		
B-0189	42.0% @10.0uM	9.0% @1.0uM		
B-0190	59.0% @10.0uM	31.0% @1.0uM		
B-0191	40.0% @1.0uM	29.0% @1.0uM		
B-0192	12.0% @10.0uM	47.0% @1.0uM		
B-0193	0.54 uM	6%@1.0uM		
B-0194	1.31 uM	22%@1.0uM		
B-0195	1.03 uM	55%@1.0uM		
B-0196	2.24 uM	>1.0uM		
B-0197	2.0 uM	14%@1.0uM		
B-0198	1.2 uM	2%@1.0uM		
B-0199	1.34 uM	3%@1.0uM		
B-0200	1.31 uM	16%@1.0uM		
B-0201	0.29 uM	59%@1.0uM		
B-0202	0.55 uM	2.26 uM		
B-0203	0.16 uM	65%@1.0uM		
B-0204	0.21 uM	48%@1.0uM		
B-0205	0.096 uM	54%@1.0uM		
B-0206	5.76 uM	14%@1.0uM		
B-0207	0.12 uM	52%@1.0uM		
B-0208	0.067 uM	>1.0uM		
B-0209	0.29 uM	8%@1.0uM		
B-0210	0.057 uM	67%@1.0uM		

SUBSTITUTE SHEET (RULE 28)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0211	0.25 uM	30% @ 1.0uM		
B-0212	0.12 uM	28% @ 1.0uM		
B-0213	0.31 uM	39% @ 1.0uM		
B-0214	0.16 uM	50% @ 1.0uM		
B-0215	0.11 uM	51% @ 1.0uM		
B-0216	0.56 uM	>1.0uM		
B-0217	0.55 uM	>1.0uM		
B-0218	0.53 uM	18% @ 1.0uM		
B-0219	0.91 uM	18% @ 1.0uM		
B-0220	0.13 uM	40% @ 1.0uM		
B-0221	2.4 uM	>1.0uM		
B-0222	0.4uM	29.0% @ 1.0uM		
B-0223	0.2uM	1.0% @ 1.0uM		
B-0224	<0.1uM	93.0% @ 1.0uM		
B-0225	0.047uM	37.0% @ 1.0uM		
B-0226	0.074uM	20.0% @ 1.0uM		
B-0227	0.045uM	1.0% @ 1.0uM		
B-0228	0.15uM	44.0% @ 1.0uM		
B-0229	<0.1uM	61.0% @ 1.0uM		
B-0230	0.041uM	30.0% @ 1.0uM		
B-0231	0.055uM	40.0% @ 1.0uM		
B-0232	0.048uM	24.0% @ 1.0uM		
B-0233	0.095uM	43.0% @ 1.0uM		
B-0234	0.11uM	68.0% @ 1.0uM		
B-0235	1.31uM	90.0% @ 1.0uM		
B-0236	0.077uM	46.0% @ 1.0uM		
B-0237	0.13uM	60.0% @ 1.0uM		
B-0238	0.47uM	82.0% @ 1.0uM		
B-0239	5.73uM	84.0% @ 1.0uM		
B-0240	0.2uM	70.0% @ 1.0uM		
B-0241	0.1uM	45.0% @ 1.0uM		
B-0242	<0.1uM	78.0% @ 1.0uM		
B-0243	0.039uM	53.0% @ 1.0uM		
B-0244	0.02uM	57.0% @ 1.0uM		
B-0245	0.13uM	24.0% @ 1.0uM		
B-0246	<0.1uM	>1.0uM		
B-0247	0.082uM	75.0% @ 1.0uM		
B-0248	<0.1uM	11.0% @ 1.0uM		
B-0249	<0.1uM	75.0% @ 1.0uM		
B-0250	0.28uM	36.0% @ 1.0uM		
B-0251	0.31uM	1.0% @ 1.0uM		
B-0252	0.041uM	54.0% @ 1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0253	0.061uM	74.0%@1.0uM		
B-0254	0.12uM	59.0%@1.0uM		
B-0255	0.32uM	68.0%@1.0uM		
B-0256	<0.1uM	88.0%@1.0uM		
B-0257	1.71uM	11.0%@1.0uM		
B-0258	0.37uM	63.0%@1.0uM		
B-0259	0.35uM	58.0%@1.0uM		
B-0260	0.56uM	23.0%@1.0uM		
B-0261	0.49uM	23.0%@1.0uM		
B-0262	0.41uM	89.0%@1.0uM		
B-0263	0.62uM	64.0%@1.0uM		
B-0264	0.14uM	18.0%@1.0uM		
B-0265	0.92uM	24.0%@1.0uM		
B-0266	0.25uM	24.0%@1.0uM		
B-0267	0.48uM	11.0%@1.0uM		
B-0268	3.39uM	19.0%@1.0uM		
B-0269	9.81uM	19.0%@1.0uM		
B-0270	5.79uM	13.0%@1.0uM		
B-0271	7.55uM	12.0%@1.0uM		
B-0272	1.81uM	48.0%@1.0uM		
B-0273	5.03uM	13.0%@1.0uM		
B-0274	2.68uM	25.0%@1.0uM		
B-0275	2.67uM	33.0%@1.0uM		
B-0276	1.25uM	26.0%@1.0uM		
B-0277	0.68uM	34.0%@1.0uM		
B-0278	1.26uM	36.0%@1.0uM		
B-0279	1.39uM	33.0%@1.0uM		
B-0280	0.86uM	18.0%@1.0uM		
B-0281	7.37uM	24.0%@1.0uM		
B-0282	0.75uM	38.0%@1.0uM		
B-0283	6.66uM	29.0%@1.0uM		
B-0284	0.083uM	65.0%@1.0uM		
B-0285	4.57uM	29.0%@1.0uM		
B-0286	0.33uM	50.0%@1.0uM		
B-0287	4.0uM	22.0%@1.0uM		
B-0288	4.46uM	26.0%@1.0uM		
B-0289	0.15uM	55.0%@1.0uM		
B-0290	0.66uM	44.0%@1.0uM		
B-0291	1.33uM	20.0%@1.0uM		
B-0292	0.22uM	28.0%@1.0uM		
B-0293	0.66uM	53.0%@1.0uM		
B-0294	0.68uM	45.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0295	0.82uM	45.0% @ 1.0uM		
B-0296	8.03uM	36.0% @ 1.0uM		
B-0297	0.78uM	30.0% @ 1.0uM		
B-0298	0.58uM	48.0% @ 1.0uM		
B-0299	0.87uM	54.0% @ 1.0uM		
B-0300	0.78uM	32.0% @ 1.0uM		
B-0301	0.19uM	50.0% @ 1.0uM		
B-0302	4.02uM	24.0% @ 1.0uM		
B-0303	0.22uM	10.0% @ 1.0uM		
B-0304	0.56uM	28.0% @ 1.0uM		
B-0305				
B-0306				
B-0307				
B-0308				
B-0309				
B-0310				
B-0311				
B-0312				
B-0313				
B-0314				
B-0315				
B-0316				
B-0317				
B-0318				
B-0319				
B-0320				
B-0321				
B-0322				
B-0323				
B-0324				
B-0325				
B-0326				
B-0327				
B-0328				
B-0329				
B-0330				
B-0331				
B-0332				
B-0333				
B-0334				
B-0335				
B-0336				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0337				
B-0338				
B-0339				
B-0340				
B-0341				
B-0342				
B-0343				
B-0344				
B-0345				
B-0346				
B-0347				
B-0348				
B-0349				
B-0350				
B-0351				
B-0352				
B-0353	1.37uM	55%@1.0uM		
B-0354	1.0uM	0.66uM	51%@30mpk@-6h	54%@3mpk@-4h
B-0355	0.75uM	40.0%@1.0uM		
B-0356	0.66uM	24.0%@1.0uM		
B-0357	1.46uM	0.66uM		
B-0358	0.37uM	17.0%@1.0uM		
B-0359	0.45uM	47.0%@1.0uM		
B-0360	1.6uM	19.0%@1.0uM		
B-0361	0.33uM	46.0%@1.0uM		
B-0362	0.52uM	27.0%@1.0uM		
B-0363	4.67uM	25.0%@1.0uM		
B-0364	1.44uM	27.0%@1.0uM		
B-0365	0.96uM	27.0%@1.0uM		
B-0366	0.7uM	46.0%@1.0uM		
B-0367	1.0uM	23.0%@1.0uM		
B-0368	1.0uM	0.64uM	37%@30mpk@-6h	
B-0369	0.16uM	57.0%@1.0uM		
B-0370	0.65uM	28.0%@1.0uM		
B-0371	0.49uM	28.0%@1.0uM		
B-0372	0.35uM	29.0%@1.0uM		
B-0373	0.45uM	18.0%@1.0uM		
B-0374	1.38uM	12.0%@1.0uM		
B-0375	1.0uM	19.0%@1.0uM		
B-0376	2.99uM	12.0%@1.0uM		
B-0377	1.29uM	36.0%@1.0uM		
B-0378	1.1uM	36.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0379	0.53uM	24.0%@1.0uM		
B-0380	1.41uM	32.0%@1.0uM		
B-0381	0.22uM	47.0%@1.0uM		
B-0382	0.41uM	32.0%@1.0uM		
B-0383	1.43uM	10.0%@1.0uM		
B-0384	4.02uM	16.0%@1.0uM		
B-0385	0.057uM	0.9uM	30%@30mpk@-6h	0%@3mpk@-4h
B-0386	0.13uM	54.0%@1.0uM		
B-0387	0.41uM	52.0%@1.0uM		
B-0388	<0.1uM	36.0%@1.0uM		
B-0389	0.01uM	0.05uM		62%@3mpk@-4h
B-0390	0.089uM	55.0%@1.0uM		
B-0391	0.86uM	18.0%@1.0uM		
B-0392	0.13uM	57.0%@1.0uM		
B-0393	0.043uM	66.0%@1.0uM		
B-0394	0.13uM	45.0%@1.0uM		
B-0395	0.087uM	48.0%@1.0uM		
B-0396	0.097uM	0.44uM		
B-0397	0.17uM	41.0%@1.0uM		
B-0398	0.054uM	66.0%@1.0uM		
B-0399	0.14uM	39.0%@1.0uM		
B-0400	0.16uM	25.0%@1.0uM		
B-0401	0.46uM	52.0%@1.0uM		
B-0402	0.14uM	1.51uM		
B-0403	1.77uM	2.42uM		
B-0404	0.31uM	48.0%@1.0uM		
B-0405	0.79uM	30.0%@1.0uM		
B-0406	0.54uM	35.0%@1.0uM		
B-0407	0.76uM	27.0%@1.0uM		
B-0408	0.5uM	50.0%@1.0uM		
B-0409	0.53uM	30.0%@1.0uM		
B-0410	0.38uM	44.0%@1.0uM		
B-0411	0.62uM	50.0%@1.0uM		
B-0412	0.24uM	48.0%@1.0uM		
B-0413	0.18uM	55.0%@1.0uM		
B-0414	2.54uM	25.0%@1.0uM		
B-0415	0.42uM	43.0%@1.0uM		
B-0416	0.32uM	34.0%@1.0uM		
B-0417	0.91uM	28.0%@1.0uM		
B-0418	0.22uM	27.0%@1.0uM		
B-0419	0.85uM	41.0%@1.0uM		
B-0420	0.83uM	49.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0421	0.46uM	57.0%@1.0uM		
B-0422	<0.1uM	40.0%@1.0uM		
B-0423	0.18uM	33.0%@1.0uM		
B-0424	0.083uM	32.0%@1.0uM		
B-0425	0.26uM	54.0%@1.0uM		
B-0426	0.055uM	0.74uM		41%@3mpk@-4h
B-0427	0.63uM	39.0%@1.0uM		
B-0428	0.99uM	27.0%@1.0uM		
B-0429	0.27uM	45.0%@1.0uM		
B-0430	0.29uM	75.0%@1.0uM		
B-0431	0.21uM	64.0%@1.0uM		
B-0432	<0.1uM	89.0%@1.0uM		
B-0433	<0.1uM	92.0%@1.0uM		
B-0434	0.12uM	65.0%@1.0uM		
B-0435	0.3uM	61.0%@1.0uM		
B-0436	1.11uM	71.0%@1.0uM		
B-0437	0.58uM	59.0%@1.0uM		
B-0438	<0.1uM	91.0%@1.0uM		
B-0439	2.12uM	65.0%@1.0uM		
B-0440	0.66uM	63.0%@1.0uM		
B-0441	0.8uM	58.0%@1.0uM		
B-0442	<0.1uM	91.0%@1.0uM		
B-0443	2.01uM	71.0%@1.0uM		
B-0444	1.01uM	51.0%@1.0uM		
B-0445	<0.1uM	83.0%@1.0uM		
B-0446	0.78uM	80.0%@1.0uM		
B-0447	0.19uM	71.0%@1.0uM		
B-0448	0.4uM	79.0%@1.0uM		
B-0449	0.83uM	81.0%@1.0uM		
B-0450	0.26uM	81.0%@1.0uM		
B-0451	0.071uM	83.0%@1.0uM	42%@30mpk@-6h	
B-0452	0.7uM	75.0%@1.0uM		
B-0453	0.47uM	75.0%@1.0uM		
B-0454	0.11uM	80.0%@1.0uM		
B-0455	<0.1uM	95.0%@1.0uM		36%@3mpk%-4h
B-0456	1.81uM	67.0%@1.0uM		
B-0457	0.089uM	81.0%@1.0uM		
B-0458	0.033uM	70.0%@1.0uM		
B-0459	0.099uM	76.0%@1.0uM		
B-0460	0.061uM	92.0%@1.0uM		
B-0461	0.025uM	96.0%@1.0uM		
B-0462	<0.1uM	97.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0463	0.052uM	95.0%@1.0uM		
B-0464	<0.1uM	91.0%@1.0uM		
B-0465	0.084uM	98.0%@1.0uM		
B-0466	<0.1uM	98.0%@1.0uM		0%@3mpk@-4h
B-0467	<0.1uM	77.0%@1.0uM		
B-0468	0.031uM	93.0%@1.0uM		
B-0469	0.056uM	92.0%@1.0uM		
B-0470	0.063uM	92.0%@1.0uM		
B-0471	0.027uM	97.0%@1.0uM		
B-0472	0.19uM	54.0%@1.0uM		
B-0473	0.004uM	95.0%@1.0uM		
B-0474	0.024uM	86.0%@1.0uM		
B-0475	0.21uM	74.0%@1.0uM		
B-0476	0.56uM	69.0%@1.0uM		
B-0477	1.48uM	96.0%@1.0uM		
B-0478	0.034uM	87.0%@1.0uM		
B-0479	0.031uM	90.0%@1.0uM		15%@3mpk@-4h
B-0480	0.12uM	88.0%@1.0uM		
B-0481	0.014uM	95.0%@1.0uM		56%@3mpk@-4h
B-0482	0.97uM	68.0%@1.0uM		
B-0483	0.57uM	68.0%@1.0uM		
B-0484	0.28uM	62.0%@1.0uM		
B-0485	0.04uM	95.0%@1.0uM		
B-0486	0.24uM	80.0%@1.0uM		
B-0487	0.11uM	89.0%@1.0uM		54%@3mpk@-4h
B-0488	0.62uM	88.0%@1.0uM		
B-0489	0.3uM	80.0%@1.0uM		
B-0490	0.91uM	74.0%@1.0uM		
B-0491	0.43uM	66.0%@1.0uM		
B-0492	0.069uM	42.0%@1.0uM		
B-0493	0.3uM	36.0%@1.0uM		
B-0494	0.13uM	30.0%@1.0uM		
B-0495	0.12uM	25.0%@1.0uM		
B-0496	0.83uM	16.0%@1.0uM		
B-0497	0.44uM	31.0%@1.0uM		
B-0498	0.33uM	11.0%@1.0uM		
B-0499	0.39uM	37.0%@1.0uM		
B-0500	0.26uM	41.0%@1.0uM		
B-0501	0.049uM	52.0%@1.0uM		
B-0502	0.065uM	48.0%@1.0uM		
B-0503	0.16uM	73.0%@1.0uM		
B-0504	0.4uM	43.0%@1.0uM		

SUBSTITUTE SHEET (RULE 28)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0505	0.28uM	44.0%@1.0uM		
B-0506	0.94uM	43.0%@1.0uM		
B-0507	0.18uM	75.0%@1.0uM		
B-0508	2.0uM	48.0%@1.0uM		
B-0509	0.1uM	86.0%@1.0uM		
B-0510	0.69uM	61.0%@1.0uM		
B-0511	0.007uM	90.0%@1.0uM		
B-0512	1.0uM	53.0%@1.0uM		
B-0513	0.72uM	52.0%@1.0uM		
B-0514	0.14uM	87.0%@1.0uM		
B-0515	0.42uM	61.0%@1.0uM		
B-0516	0.37uM	84.0%@1.0uM		
B-0517	0.094uM	52.0%@1.0uM		
B-0518	0.11uM	64.0%@1.0uM		
B-0519	0.043uM	87.0%@1.0uM		
B-0520	0.4uM	67.0%@1.0uM		
B-0521	1.37uM	52.0%@1.0uM		
B-0522	0.15uM	75.0%@1.0uM		
B-0523	0.19uM	83.0%@1.0uM		
B-0524	0.4uM	77.0%@1.0uM		
B-0525	0.16uM	76.0%@1.0uM		
B-0526	0.031uM	87.0%@1.0uM		
B-0527	1.09uM	63.0%@1.0uM		
B-0528	0.14uM	70.0%@1.0uM		
B-0529	0.11uM	73.0%@1.0uM		
B-0530	5.53uM	45.0%@1.0uM		
B-0531	0.5uM	48.0%@1.0uM		
B-0532	0.45uM	1.01uM	41%@30mpk@-6h	
B-0533	1.23uM	47.0%@1.0uM		
B-0534	0.41uM	54.0%@1.0uM		
B-0535	0.44uM	0.87uM		
B-0536	0.46uM	0.15uM		
B-0537	3.44uM	51.0%@1.0uM		
B-0538	1.13uM	45.0%@1.0uM		
B-0539	2.84uM	21.0%@1.0uM		
B-0540	3.62uM	54.0%@1.0uM		
B-0541	3.24uM	28.0%@1.0uM		
B-0542	1.55uM	50.0%@1.0uM		
B-0543	1.56uM	43.0%@1.0uM		
B-0544	1.12uM	27.0%@1.0uM		
B-0545	1.06uM	41.0%@1.0uM		
B-0546	1.04uM	18.0%@1.0uM		
B-0547	1.24uM	21.0%@1.0uM		
B-0548	1.77uM	28.0%@1.0uM		
B-0549	2.22uM	22.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0550	2.41uM	14.0%@1.0uM		
B-0551	1.08uM	56.0%@1.0uM		
B-0552	0.13uM	46.0%@1.0uM		
B-0553	1.44uM	47.0%@1.0uM		
B-0554	2.58uM	20.0%@1.0uM		
B-0555	1.87uM	34.0%@1.0uM		
B-0556	0.49uM	39.0%@1.0uM		
B-0557	1.37uM	32.0%@1.0uM		
B-0558	0.85uM	33.0%@1.0uM		
B-0559	0.53uM	49.0%@1.0uM		
B-0560	2.57uM	31.0%@1.0uM		
B-0561	2.07uM	40.0%@1.0uM		
B-0562	0.22uM	0.3uM		5%@3mpk@ -4h
B-0563	0.18uM	0.13uM		
B-0564	0.82uM	58%@1.0uM		
B-0565	0.23uM	0.59uM		
B-0566	<0.1uM	0.17uM		0%@3mpk@ -4h
B-0567	0.14uM	0.28uM		
B-0568	1.22uM	46.0%@1.0uM		
B-0569	0.15uM	0.26uM		
B-0570	0.27uM	46.0%@1.0uM		
B-0571	0.38uM	44.0%@1.0uM		
B-0572	0.27uM	41.0%@1.0uM		
B-0573	0.36uM	1.7uM		
B-0574	0.13uM	0.66uM		37%@3mpk@ -4h
B-0575	0.032uM	0.17uM		
B-0576	0.068uM	0.39uM		65%@3mpk@ -4h
B-0577	0.091uM	66.0%@1.0uM		
B-0578	1.88uM	47.0%@1.0uM		
B-0579	0.11uM	79.0%@1.0uM		
B-0580	2.23uM	0.84uM		
B-0581	0.26uM	2.17uM		
B-0582	1.03uM	37.0%@1.0uM		
B-0583	3.93uM	26.0%@1.0uM		
B-0584	0.66uM	54.0%@1.0uM		
B-0585	0.83uM	79.0%@1.0uM	50%@30mpk@ -6h	
B-0586	0.81uM	51.0%@1.0uM		
B-0587	6.84uM	38%@1.0uM		
B-0588	12.8uM	42%@1.0uM		
B-0589	1.71uM	42%@1.0uM		
B-0590	1.57uM	38.0uM		
B-0591	3.59uM	29.0%@1.0uM		
B-0592	1.62uM	45.0%@1.0uM		
B-0593	1.22uM	36.0%@1.0uM		
B-0594	-	41.0%@1.0uM		
B-0595	2.42uM	22.0%@1.0uM		
B-0596	20.0uM	41.0%@1.0uM		
B-0597	1.68uM	63.0%@1.0uM		
B-0598	2.12uM	50.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0599	4.16uM	21.0% @ 1.0uM		
B-0600	0.002uM	28.0% @ 1.0uM		
B-0601	0.089uM	1.31uM		43% @ 3mpk% -4h
B-0602	0.97uM	61.0% @ 1.0uM		
B-0603	0.09uM	51.0% @ 1.0uM		
B-0604	0.3uM	20.0% @ 1.0uM		
B-0605	0.18uM	47.0% @ 1.0uM		
B-0606	0.17uM	53.0% @ 1.0uM		
B-0607	2.79uM	70.0% @ 1.0uM		
B-0608	0.059uM	73.0% @ 1.0uM		
B-0609	<0.1uM	87.0% @ 1.0uM		
B-0610	<0.1uM	88.0% @ 1.0uM		
B-0611	0.65uM	60.0% @ 1.0uM		
B-0612	0.16uM	60.0% @ 1.0uM		
B-0613	0.17uM	76.0% @ 1.0uM		
B-0614	0.76uM	70.0% @ 1.0uM		0% @ 3mpk@ -4h
B-0615	0.08uM	83.0% @ 1.0uM		
B-0616	0.38uM	87.0% @ 1.0uM		
B-0617	0.045uM	92.0% @ 1.0uM		
B-0618	0.37uM	80.0% @ 1.0uM		
B-0619	<0.1uM	88.0% @ 1.0uM		
B-0620	1.59uM	58.0% @ 1.0uM		
B-0621	0.36uM	68.0% @ 1.0uM		
B-0622	0.076uM	78.0% @ 1.0uM		
B-0623	0.12uM	76.0% @ 1.0uM		
B-0624	0.085uM	54.0% @ 1.0uM		
B-0625	0.023uM	88.0% @ 1.0uM		
B-0626	<0.1uM	85.0% @ 1.0uM		
B-0627	0.25uM	69.0% @ 1.0uM		
B-0628	0.023uM	72.0% @ 1.0uM		
B-0629	0.2uM	79.0% @ 1.0uM		
B-0630	0.06uM	77.0% @ 1.0uM		
B-0631	0.065uM	81.0% @ 1.0uM		
B-0632	<0.1uM	79.0% @ 1.0uM		
B-0633	0.6uM	80.0% @ 1.0uM		
B-0634	0.6uM	40.0% @ 1.0uM		
B-0635	0.15uM	55.0% @ 1.0uM		
B-0636	<0.1uM	86.0% @ 1.0uM		
B-0637	0.11uM	92.0% @ 1.0uM		
B-0638	0.25uM	89.0% @ 1.0uM		
B-0639	0.051uM	93.0% @ 1.0uM		50% @ 3mpk@ -4h
B-0640	0.36uM	94.0% @ 1.0uM		
B-0641	0.58uM	65.0% @ 1.0uM		
B-0642	0.49uM	90.0% @ 1.0uM		
B-0643	0.069uM	85.0% @ 1.0uM		0% @ 3mpk@ -4h
B-0644	0.058uM	89.0% @ 1.0uM		
B-0645	0.58uM	80.0% @ 1.0uM		
B-0646	0.26uM	94.0% @ 1.0uM		
B-0647	1.61uM	76.0% @ 1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0648	<0.1uM	83.0%@1.0uM		
B-0649	0.83uM	39.0%@1.0uM		
B-0650	0.006uM	95.0%@1.0uM		8%@3mpk@-4h
B-0651	1.78uM	81.0%@1.0uM		
B-0652	0.19uM	83.0%@1.0uM		
B-0653	2.01uM	74.0%@1.0uM		
B-0654	5.97uM	78.0%@1.0uM		
B-0655	1.25uM	76.0%@1.0uM		
B-0656	0.007uM	95.0%@1.0uM		28%@3mpk@-4h
B-0657	0.17uM	83.0%@1.0uM		
B-0658	1.14uM	91.0%@1.0uM		
B-0659	2.64uM	87.0%@1.0uM		
B-0660	0.088uM	92.0%@1.0uM		
B-0661	<0.1uM	90.0%@1.0uM		
B-0662	<0.1uM	95.0%@1.0uM		
B-0663	0.88uM	74.0%@1.0uM		
B-0664	0.39uM	80.0%@1.0uM		
B-0665	0.47uM	72.0%@1.0uM		
B-0666	0.17uM	73.0%@1.0uM		
B-0667	0.83uM	75.0%@1.0uM		
B-0668	0.27uM	78.0%@1.0uM		
B-0669	0.89uM	34.0%@1.0uM		
B-0670	3.15uM	32.0%@1.0uM		
B-0671	6.38uM	36.0%@1.0uM		
B-0672	6.59uM	32.0%@1.0uM		
B-0673	8.54uM	48.0%@1.0uM		
B-0674	2.81uM	42.0%@1.0uM		
B-0675	5.42uM	3.0%@1.0uM		
B-0676	2.09uM	22.0%@1.0uM		
B-0677	1.63uM	25.0%@1.0uM		
B-0678	0.38uM	52.0%@1.0uM		
B-0679	0.062uM	45.0%@1.0uM		
B-0680	0.42uM	67.0%@1.0uM		
B-0681	1.96uM	17.0%@1.0uM		
B-0682	0.76uM	39.0%@1.0uM		
B-0683	13.0uM	32.0%@1.0uM		
B-0684	0.54uM	68.0%@1.0uM		
B-0685	15.4uM	33.0%@1.0uM		
B-0686	0.42uM	59.0%@1.0uM		
B-0687	10.1uM	15.0%@1.0uM		
B-0688	0.66uM	58.0%@1.0uM		
B-0689	14.6uM	27.0%@1.0uM		
B-0690	27.1uM	36.0%@1.0uM		
B-0691	0.16uM	48.0%@1.0uM		
B-0692	0.38uM	29.0%@1.0uM		
B-0693	0.39uM	28.0%@1.0uM		
B-0694	0.62uM	21.0%@1.0uM		
B-0695	0.23uM	32.0%@1.0uM		
B-0696	0.085uM	35.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0697	0.45uM	44.0%@1.0uM		
B-0698	2.33uM	43.0%@1.0uM		
B-0699	0.34uM	31.0%@1.0uM		
B-0700	0.24uM	56.0%@1.0uM		
B-0701	0.39uM	45.0%@1.0uM		
B-0702	0.036uM	39.0%@1.0uM		
B-0703	0.12uM	39.0%@1.0uM		
B-0704	2.19uM	29.0%@1.0uM		
B-0705	0.44uM	21.0%@1.0uM		
B-0706	0.44uM	32.0%@1.0uM		
B-0707	1.7uM			
B-0708	2.1uM			
B-0709	0.84uM			
B-0710	1.99uM			
B-0711	1.99uM			
B-0712	2.9uM			
B-0713	4.3uM			
B-0714	3.7uM			
B-0715	3.2uM			
B-0716	4.6uM			
B-0717	4.3uM			
B-0718	1.4uM			
B-0719	3.4uM			
B-0720	1.3uM			
B-0721	3.8uM			
B-0722	0.07uM	>1.0uM		
B-0723	0.47uM			
B-0724	0.06uM	17.0%@1.0uM		
B-0725	9.7uM			
B-0726	1.4uM			
B-0727	0.51uM			
B-0728	20.0uM			
B-0729	0.87uM			
B-0730	0.25uM	11.0%@1.0uM		
B-0731	0.87uM	>1.0uM		
B-0732	14.0uM			
B-0733	32.0uM			
B-0734	0.92uM			
B-0735	1.0uM			
B-0736	26.0uM			
B-0737	2.6uM			
B-0738	2.7uM			
B-0739	4.1uM			
B-0740	4.4uM			
B-0741	26.0uM			
B-0742	2.2uM			
B-0743	1.2uM			
B-0744	23.0uM			
B-0745	6.0uM			

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0746	0.01uM	22.0%@1.0uM		
B-0747	1.1uM			
B-0748	1.2uM			
B-0749	4.4uM			
B-0750	0.92uM			
B-0751	1.6uM			
B-0752	0.33uM			
B-0753	0.37uM			
B-0754	0.55uM			
B-0755	2.3uM			
B-0756	0.94uM			
B-0757	0.54uM	16.0%@1.0uM		
B-0758	1.5uM			
B-0759	0.3uM			
B-0760	0.01uM	13.0%@1.0uM		
B-0761	<0.1uM			
B-0762	0.13uM	5.0%@1.0uM		
B-0763	0.015uM	17.0%@1.0uM		
B-0764	0.67uM	26.0%@1.0uM		
B-0765	0.3uM	29.0%@1.0uM		
B-0766	0.95uM			
B-0767	0.08uM			
B-0768	1.4uM			
B-0769	12.7uM			
B-0770	2.3uM			
B-0771	0.5uM			
B-0772	0.8uM			
B-0773	14.0uM			
B-0774	1.5uM			
B-0775	0.6uM	>1.0uM		
B-0776	0.9uM	>1.0uM		
B-0777	21.0uM			
B-0778	51.0uM			
B-0779	0.5uM			
B-0780	1.1uM			
B-0781	48.0uM			
B-0782	22.0uM			
B-0783	8.0uM			
B-0784	7.0uM			
B-0785	23.0uM			
B-0786	24.0uM			
B-0787	1.5uM			
B-0788	1.2uM			
B-0789	33.0uM			
B-0790	1.0uM	4.0%@1.0uM		
B-0791	0.3uM	>1.0uM		
B-0792	1.1uM			
B-0793	0.3uM			
B-0794	2.9uM	2.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM-or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0795	1.9uM	11.0% @ 1.0uM		
B-0796	1.4uM			
B-0797	1.04uM	-		
B-0798	1.73uM	-		
B-0799	-	>1.0uM		
B-0800	1.01uM	>1.0uM		
B-0801	0.67uM	>1.0uM		
B-0802	-	>1.0uM		
B-0803	0.057uM	53.0% @ 1.0uM		
B-0804	0.3uM	32.0% @ 1.0uM		
B-0805	0.71uM	>1.0uM		
B-0806	3.28uM	>1.0uM		
B-0807	10.8uM	-		
B-0808	3.09uM	>1.0uM		
B-0809	1.22uM	7.0% @ 1.0uM		
B-0810	1.11uM	>1.0uM		
B-0811	2.79uM	2.0% @ 1.0uM		
B-0812	2.12uM	>1.0uM		
B-0813	3.02uM	>1.0uM		
B-0814	-	>1.0uM		
B-0815	2.11uM	>1.0uM		
B-0816	3.46uM	>1.0uM		
B-0817	3.07uM	33.0% @ 1.0uM		
B-0818	4.97uM	>1.0uM		
B-0819	1.08uM	>1.0uM		
B-0820	1.64uM	3.0% @ 1.0uM		
B-0821	1.44uM	-		
B-0822	1.33uM	-		
B-0823	2.39uM	>1.0uM		
B-0824	3.41uM	-		
B-0825	-	-		
B-0826	1.74uM	-		
B-0827	15.6uM	-		
B-0828	7.9uM	-		
B-0829	0.61uM	65.0% @ 1.0uM		
B-0830	0.54uM	34.0% @ 1.0uM		
B-0831	0.9uM	>1.0uM		
B-0832	1.49uM	-		
B-0833	0.95uM	23.0% @ 1.0uM		
B-0834	1.25uM	-		
B-0835	-	-		
B-0836	1.24uM	-		
B-0837	1.96uM	>1.0uM		
B-0838	3.1uM	-		
B-0839	4.3uM	-		
B-0840	0.63uM	47.0% @ 1.0uM		
B-0841	0.32uM	36.0% @ 1.0uM		
B-0842	0.74uM	63.0% @ 1.0uM		
B-0843	0.61uM	>1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib. @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0844	0.4uM	25.0%@1.0uM		
B-0845	1.78uM	-		
B-0846	1.8uM	-		
B-0847	0.73uM	21.0%@1.0uM		
B-0848	1.56uM	-		
B-0849	1.25uM	-		
B-0850	1.81uM	-		
B-0851	0.91uM	39.0%@1.0uM		
B-0852	1.02uM	-		
B-0853	-	38.0%@1.0uM		
B-0854	-	25.0%@1.0uM		
B-0855	-	8.0%@1.0uM		
B-0856	-	38.0%@1.0uM		
B-0857	6.25uM	-		
B-0858	2.1uM	48.0%@1.0uM		
B-0859	39.5uM	-		
B-0860	38.1uM	-		
B-0861	1.32uM	12.0%@1.0uM		
B-0862	2.15uM	4.0%@1.0uM		
B-0863	0.81uM	25.0%@1.0uM		
B-0864	0.39uM	40.%@1.0uM		
B-0865	0.66uM	46.0%@1.0uM		
B-0866	1.38uM	28.0%@1.0uM		
B-0867	0.62uM	>1.0uM		
B-0868	3.28uM	8.0%@1.0uM		
B-0869	4.19uM	>1.0uM		
B-0870	3.13uM	>1.0uM		
B-0871	1.9uM	>1.0uM		
B-0872	3.13uM	3.0%@1.0uM		
B-0873	6.92uM	>1.0uM		
B-0874	1.92uM	>1.0uM		
B-0875	2.13uM	8%@1.0uM		
B-0876	0.89uM	>1.0uM		
B-0877	1.17uM	13.0%@1.0uM		
B-0878	0.65uM	19.0%@1.0uM		
B-0879	0.87uM	1.0%@1.0uM		
B-0880	0.15uM	40.0%@1.0uM		
B-0881	1.36uM	>1.0uM		
B-0882	1.48uM	9%@1.0uM		
B-0883	1.06uM	>1.0uM		
B-0884	1.89uM	-		
B-0885				
B-0886				
B-0887				
B-0888				
B-0889				
B-0890				
B-0891				
B-0892				

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0893				
B-0894				
B-0895				
B-0896				
B-0897				
B-0898				
B-0899				
B-0900				
B-0901				
B-0902				
B-0903				
B-0904				
B-0905				
B-0906				
B-0907				
B-0908				
B-0909				
B-0910				
B-0911				
B-0912				
B-0913				
B-0914				
B-0915				
B-0916				
B-0917				
B-0918				
B-0919				
B-0920				
B-0921				
B-0922				
B-0923				
B-0924				
B-0925				
B-0926				
B-0927				
B-0928				
B-0929				
B-0930				
B-0931				
B-0932				
B-0933	47.0%@1.0uM	37.0%@1.0uM		
B-0934	67.0%@1.0uM	36.0%@1.0uM		
B-0935	69.0%@1.0uM	54.0%@1.0uM		
B-0936	69.0%@1.0uM	>1.0uM		
B-0937	64.0%@1.0uM	1.74uM		
B-0938	51.0%@1.0uM	29.0%@1.0uM		
B-0939	78.0%@1.0uM	14.0%@1.0uM		
B-0940	56.0%@1.0uM	22.0%@1.0uM		
B-0941	81.0%@1.0uM	25.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0942	82.0% @ 1.0uM	2.0% @ 1.0uM		
B-0943	63.0% @ 10.0uM	24.0% @ 1.0uM		
B-0944	45.0% @ 1.0uM	27.0% @ 1.0uM		
B-0945	96.0% @ 1.0uM	0.93uM		
B-0946	76.0% @ 1.0uM	31.0% @ 1.0uM		
B-0947	69.0% @ 1.0uM	34.0% @ 1.0uM		
B-0948	68.0% @ 1.0uM	1.81uM		
B-0949	90.0% @ 1.0uM	17.0% @ 1.0uM		
B-0950	81.0% @ 1.0uM	0.58uM		
B-0951	82.0% @ 1.0uM	20.0% @ 1.0uM		
B-0952	44.0% @ 1.0uM	21.0% @ 1.0uM		
B-0953	63.0% @ 1.0uM	25.0% @ 1.0uM		
B-0954	62.0% @ 1.0uM	0.52uM		
B-0955	49.0% @ 1.0uM	0.54uM		
B-0956	56.0% @ 1.0uM	1.33uM		
B-0957	79.0% @ 1.0uM	22.0% @ 1.0uM		
B-0958	74.0% @ 1.0uM	0.38uM		
B-0959	83.0% @ 1.0uM	39.0% @ 1.0uM		
B-0960	48.0% @ 1.0uM	4.0% @ 1.0uM		
B-0961	79.0% @ 1.0uM	23.0% @ 1.0uM		
B-0962	85.0% @ 1.0uM	2.71uM		
B-0963	76.0% @ 1.0uM	39.0% @ 1.0uM		
B-0964	94.0% @ 1.0uM	5.0uM		
B-0965	74.0% @ 1.0uM	1.1uM		
B-0966	50.0% @ 1.0uM	5.0% @ 1.0uM		
B-0967	80.0% @ 1.0uM	29.0% @ 1.0uM		
B-0968	35.0% @ 1.0uM	26.0% @ 1.0uM		
B-0969	63.0% @ 1.0uM	35.0% @ 1.0uM		
B-0970	76.0% @ 10.0uM	0.88uM		
B-0971	61.0% @ 1.0uM	39.0% @ 1.0uM		
B-0972	85.0% @ 1.0uM	2.0% @ 1.0uM		
B-0973	66.0% @ 10.0uM	48.0% @ 1.0uM		
B-0974	57.0% @ 1.0uM	47.0% @ 1.0uM		
B-0975	82.0% @ 1.0uM	32.0% @ 1.0uM		
B-0976	79.0% @ 1.0uM	36.0% @ 1.0uM		
B-0977	60.0% @ 1.0uM	26.0% @ 1.0uM		
B-0978	59.0% @ 1.0uM	36.0% @ 1.0uM		
B-0979	56.0% @ 10.0uM	23.0% @ 1.0uM		
B-0980	68.0% @ 1.0uM	31.0% @ 1.0uM		
B-0981	62.0% @ 1.0uM	57.0% @ 1.0uM		
B-0982	65.0% @ 1.0uM	23.0% @ 1.0uM		
B-0983	75.0% @ 1.0uM	0.8uM		
B-0984	60.0% @ 1.0uM	51.0% @ 1.0uM		
B-0985	86.0% @ 1.0uM	0.75uM		
B-0986	70.0% @ 1.0uM	71.0% @ 1.0uM		
B-0987	78.0% @ 1.0uM	79.0% @ 1.0uM		
B-0988	72.0% @ 1.0uM	65.0% @ 1.0uM		
B-0989	85.0% @ 1.0uM	0.85uM		
B-0990		26.0% @ 1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0991	58.0%@1.0uM	33.0%@1.0uM		
B-0992	77.0%@1.0uM	45.0%@1.0uM		
B-0993	57.0%@1.0uM	73.0%@1.0uM		
B-0994	55.0%@1.0uM	43.0%@1.0uM		
B-0995	53.0%@1.0uM	14.0%@1.0uM		
B-0996	54.0%@1.0uM	27.0%@1.0uM		
B-0997	69.0%@1.0uM	22.0%@1.0uM		
B-0998	67.0%@1.0uM	25.0%@1.0uM		
B-0999	61.0%@1.0uM	24.0%@1.0uM		
B-1000	55.0%@1.0uM	42.0%@1.0uM		
B-1001	63.0%@1.0uM	31.0%@1.0uM		
B-1002	70.0%@1.0uM	41.0%@1.0uM		
B-1003	74.0%@1.0uM	29.0%@1.0uM		
B-1004	79.0%@1.0uM	45.0%@1.0uM		
B-1005	58.0%@1.0uM	23.0%@1.0uM		
B-1006	69.0%@1.0uM	38.0%@1.0uM		
B-1007	52.0%@1.0uM	34.0%@1.0uM		
B-1008	54.0%@1.0uM	23.0%@1.0uM		
B-1009	80.0%@1.0uM	55.0%@1.0uM		
B-1010	75.0%@1.0uM	1.0uM		
B-1011	72.0%@21.0uM	17.0%@1.0uM		
B-1012	-	20.0%@1.0uM		
B-1013	85.0%@1.0uM	7.0%@1.0uM		
B-1014	88.0%@1.0uM	20.0%@1.0uM		
B-1015	77.0%@1.0uM	34.0%@1.0uM		
B-1016	58.0%@1.0uM	10.0%@1.0uM		
B-1017	96.0%@1.0uM	58.0%@1.0uM		
B-1018	88.0%@1.0uM	34.0%@1.0uM		
B-1019	82.0%@1.0uM	66.0%@1.0uM		
B-1020	87.0%@1.0uM	36.0%@1.0uM		
B-1021	82.0%@1.0uM	35.0%@1.0uM		
B-1022	84.0%@1.0uM	53.0%@1.0uM		
B-1023	93.0%@1.0uM	70.0%@1.0uM		
B-1024	89.0%@1.0uM	57.0%@1.0uM		
B-1025	61.0%@1.0uM	23.0%@1.0uM		
B-1026	87.0%@1.0uM	53.0%@1.0uM		
B-1027	58.0%@1.0uM	18.0%@1.0uM		
B-1028	70.0%@1.0uM	17.0%@1.0uM		
B-1029	69.0%@1.0uM	54.0%@1.0uM		
B-1030	76.0%@1.0uM	60.0%@1.0uM		
B-1031	69.0%@1.0uM	42.0%@1.0uM		
B-1032	76.0%@1.0uM	37.0%@1.0uM		
B-1033	86.0%@1.0uM	34.0%@1.0uM		
B-1034	66.0%@1.0uM	39.0%@1.0uM		
B-1035	75.0%@1.0uM	52.0%@1.0uM		
B-1036	68.0%@1.0uM	68.0%@1.0uM		
B-1037	-	41.0%@1.0uM		
B-1038	57.0%@1.0uM	0.57uM		
B-1039	-	1.33uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1040	72.0%@1.0uM	0.38uM		
B-1041	70.0%@1.0uM	73.0%@1.0uM		
B-1042	79.0%@1.0uM	12.0%@1.0uM		
B-1043	64.0%@1.0uM	53.0%@1.0uM		
B-1044	94.0%@1.0uM	0.93uM		
B-1045	78.0%@1.0uM	25.0%@1.0uM		
B-1046	72.0%@1.0uM	66.0%@1.0uM		
B-1047	72.0%@1.0uM	58.0%@1.0uM		
B-1048	67.0%@1.0uM	19.0%@1.0uM		
B-1049	67.0%@1.0uM	65.0%@1.0uM		
B-1050	-	0.54uM		
B-1051	68.0%@1.0uM	41%@1.0uM		
B-1052	69.0%@1.0uM	66%@1.0uM		
B-1053	78.0%@1.0uM	0.4uM		
B-1054	79.0%@1.0uM	55.0%@1.0uM		
B-1055	89.0%@1.0uM	63.0%@1.0uM		
B-1056	89.0%@1.0uM	0.76uM		
B-1057	85.0%@1.0uM	0.72uM		
B-1058	0.66uM	43.0%@1.0uM		
B-1059	0.18uM	24.0%@1.0uM		
B-1060	0.11uM	32.0%@1.0uM		
B-1061	0.03uM	19.0%@1.0uM		
B-1062	<0.1uM	26.0%@1.0uM		
B-1063	0.16uM	44.0%@1.0uM		
B-1064	0.39uM	50.0%@1.0uM		
B-1065	0.56uM	40.0%@1.0uM		
B-1066	<0.1uM	39.0%@1.0uM		
B-1067	1.6uM	32.0%@1.0uM		
B-1068	0.48uM	24.0%@1.0uM		
B-1069	0.22uM	27.0%@1.0uM		
B-1070	<0.1uM	44.0%@1.0uM		
B-1071	<0.1uM	48.0%@1.0uM		
B-1072	0.38uM	28.0%@1.0uM		
B-1073	<0.1uM	21.0%@1.0uM		
B-1074	0.23uM	33.0%@1.0uM		
B-1075	0.03uM	29.0%@1.0uM		
B-1076	0.08uM	31.0%@1.0uM		
B-1077	<0.1uM	38.0%@1.0uM		
B-1078	0.26uM	48.0%@1.0uM		
B-1079	<0.1uM	40.0%@1.0uM		
B-1080	0.19uM	28.0%@1.0uM		
B-1081	<0.1uM	37.0%@1.0uM		
B-1082	<0.1uM	54.0%@1.0uM		
B-1083	<0.1uM	23.0%@1.0uM		
B-1084	0.43uM	29.0%@1.0uM		
B-1085	<0.1uM	29.0%@1.0uM		
B-1086	<0.1uM	42.0%@1.0uM		
B-1087	0.05uM	32.0%@1.0uM		
B-1088	0.73uM	49.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1089	<0.1uM	39.0%@1.0uM		
B-1090	<0.1uM	90.0%@1.0uM		
B-1091	<0.1uM	73.0%@1.0uM		
B-1092	0.27uM	85.0%@1.0uM		
B-1093	0.33uM	36.0%@1.0uM		
B-1094	0.013uM	69.0%@1.0uM		
B-1095	<0.1uM	70.0%@1.0uM		
B-1096	<0.1uM	32.0%@1.0uM		
B-1097	<0.1uM	44.0%@1.07uM		
B-1098	<0.1uM	82.0%@1.0uM		
B-1099	0.26uM	74.0%@1.0uM		
B-1100	0.22uM	56.0%@1.0uM		
B-1101	0.026uM	82.0%@1.0uM		
B-1102	0.035uM	83.0%@1.0uM		
B-1103	0.094uM	90.0%@1.0uM		
B-1104	0.12uM	69.0%@1.0uM		
B-1105	<0.1uM	84.0%@1.0uM		
B-1106	<0.1uM	86.0%@1.0uM		
B-1107	0.057uM	84.0%@1.0uM		
B-1108	0.22uM	81.0%@1.0uM		
B-1109	0.054uM	80.0%@1.0uM		
B-1110	0.47uM	64.0%@1.0uM		
B-1111	0.19uM	64.0%@1.0uM		
B-1112	0.58uM	43.0%@1.0uM		
B-1113	<0.1uM	72.0%@1.0uM		
B-1114	0.069uM	51.0%@1.0uM		
B-1115	0.024uM	89.0%@1.0uM		
B-1116	0.41uM	81.0%@1.0uM		
B-1117	0.13uM	73.0%@1.0uM		
B-1118	0.33uM	91.0%@1.0uM		
B-1119	0.35uM	80.0%@1.0uM		
B-1120	0.47uM	9.0%@1.0uM		
B-1121	3.58uM	29.0%@1.0uM		
B-1122	1.84uM	32.0%@1.0uM		
B-1123	2.93uM	27.0%@1.0uM		
B-1124	1.49uM	52.0%@1.0uM		
B-1125	0.56uM	41.0%@1.0uM		
B-1126	1.5uM	>1.0uM		
B-1127	0.71uM	7.0%@1.0uM		
B-1128	2.55uM	26.0%@1.0uM		
B-1129	1.07uM	46.0%@1.0uM		
B-1130	0.5uM	29.0%@1.0uM		
B-1131	0.076uM	34.0%@1.0uM		
B-1132	0.72uM	11.0%@1.0uM		
B-1133	0.38uM	33.0%@1.0uM		
B-1134	1.71uM	33.0%@1.0uM		
B-1135	0.23uM	38.0%@1.0uM		
B-1136	1.17uM	40.0%@1.0uM		
B-1137	0.038uM	35.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1138	1.82uM	>1.0uM		
B-1139	0.041uM	29.0%@1.0uM		
B-1140	1.68uM	39.0%@1.0uM		
B-1141	2.47uM	32.0%@1.0uM		
B-1142	0.11uM	37.0%@1.0uM		
B-1143	0.17uM	40.0%@1.0uM		
B-1144	0.44uM	72.0%@1.0uM		
B-1145	1.07uM	71.0%@1.0uM		
B-1146	0.47uM	61.0%@1.0uM		
B-1147	0.095uM	53.0%@1.0uM		
B-1148	0.43uM	61.0%@1.0uM		
B-1149	1.55uM	48.0%@1.0uM		
B-1150	0.47uM	75.0%@1.0uM		
B-1151	0.32uM	72.0%@1.0uM		
B-1152	0.73uM	53.0%@1.0uM		
B-1153	2.22uM	52.0%@1.0uM		
B-1154	0.085uM	46.0%@1.0uM		
B-1155	3.22uM	30.0%@1.0uM		
B-1156	0.27uM	78.0%@1.0uM		
B-1157	0.26uM	66.0%@1.0uM		
B-1158	74%@1.0uM	0.68uM	53%@30mpk@-6h	
B-1159	66.0%@1.0uM	1.03uM	60%@30mpk@-6h	
B-1160	79.0%@1.0uM	0.38uM		
B-1161	64.0%@1.0uM	0.93uM	40%@30mpk@-6h	45%@3mpk@-4h
B-1162	79.0%@1.0uM	0.59uM	40%@30mpk@-6h	
B-1163	74.0%@1.0uM	0.37uM		
B-1164		0.35uM		
B-1165	66.0%@1.0uM	0.99uM		
B-1166	77.0%@1.0uM	0.39uM	50%@30mpk@-6h	50%@3mpk@-4h
B-1167	70.0%@1.0uM	1.06uM		
B-1168	66.0%@1.0uM	0.63uM		
B-1169	80.0%@1.0uM	0.11uM		
B-1170	82.0%@1.0uM	0.57uM		
B-1171	78.0%@1.0uM	0.23uM		
B-1172	68.0%@1.0uM	1.95uM		
B-1173	65.0%@1.0uM	62%@1.0uM		
B-1174	80.0%@1.0uM	0.86uM		
B-1175	72.0%@1.0uM	1.83uM		
B-1176	67.0%@1.0uM	67.0%@1.0uM		
B-1177	70.0%@1.0uM	1.16uM		
B-1178	92.0%@1.0uM	1.61uM		
B-1179	86.0%@1.0uM	0.41uM		
B-1180	78.0%@1.0uM	0.53uM		
B-1181	79.0%@1.0uM	66%@1.0uM		
B-1182	72.0%@1.0uM	0.65uM		
B-1183	77.0%@1.0uM	0.2uM		
B-1184	69.0%@1.0uM	0.63uM		
B-1185	71.0%@1.0uM	0.79uM		
B-1186	83.0%@1.0uM	60%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1187	76.0%@1.0uM	1.89uM		
B-1188	-	36.0%@1.0uM		
B-1189	68.0%@1.0uM	0.83uM		
B-1190	78.0%@1.0uM	62.0%@1.0uM		
B-1191	74.0%@1.0uM	57.0%@1.0uM		
B-1192	84.0%@1.0uM	0.47uM		
B-1193	69.0%@1.0uM	65.0%@1.0uM		
B-1194	87.0%@1.0uM	0.58uM		
B-1195	52.0%@1.0uM	60.0%@1.0uM		
B-1196	74.0%@1.0uM	68.0%@1.0uM		
B-1197	77.0%@1.0uM	45.0%@1.0uM		
B-1198	92.0%@1.0uM	0.46uM		
B-1199	87.0%@1.0uM	49.0%@1.0uM		
B-1200	95.0%@1.0uM	0.64uM		
B-1201	84.0%@1.0uM	0.51uM		
B-1202	71.0%@1.0uM	58.0%@1.0uM		
B-1203	84.0%@1.0uM	58.0%@1.0uM		
B-1204	68.0%@1.0uM	59.0%@1.0uM		
B-1205	74.0%@1.0uM	46.0%@1.0uM		
B-1206	81.0%@1.0uM	0.34uM		
B-1207	90.0%@1.0uM	58.0%@1.0uM		
B-1208	82.0%@1.0uM	51.0%@1.0uM		
B-1209	86.0%@1.0uM	55.0%@1.0uM		
B-1210	82.0%@1.0uM	57.0%@1.0uM		
B-1211	88.0%@1.0uM	59.0%@1.0uM		
B-1212	90.0%@1.0uM	57.0%@1.0uM		
B-1213	84.0%@1.0uM	0.62uM		
B-1214	76.0%@1.0uM	58.0%@1.0uM		
B-1215	86.0%@1.0uM	0.23uM		
B-1216	88.0%@1.0uM	0.18uM		
B-1217	87.0%@1.0uM	0.46uM		
B-1218	88.0%@1.0uM	76.0%@1.0uM		
B-1219	85.0%@1.0uM	37.0%@1.0uM		
B-1220	81.0%@1.0uM	53.0%@1.0uM		
B-1221	82.0%@1.0uM	44.0%@1.0uM		
B-1222	65.0%@1.0uM	9.0%@1.0uM		
B-1223	80.0%@1.0uM	61.0%@1.0uM		
B-1224	82.0%@1.0uM	74.0%@1.0uM		
B-1225	89.0%@1.0uM	73.0%@1.0uM		
B-1226	89.0%@1.0uM	0.18uM		
B-1227	83.0%@1.0uM	0.22uM		
B-1228	90.0%@1.0uM	0.72uM		
B-1229	87.0%@1.0uM	0.65uM		
B-1230	90.0%@1.0uM	0.25uM		
B-1231	94.0%@1.0uM	0.56uM		
B-1232	81.0%@1.0uM	54.0%@1.0uM		
B-1233	85.0%@1.0uM	0.36uM		
B-1234	89.0%@1.0uM	0.49uM		
B-1235	0.04uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1236	0.1uM	53.0%@1.0uM		
B-1237	0.22uM	39.0%@1.0uM		
B-1238	0.14uM	16.0%@1.0uM		
B-1239	<0.1uM	38.0%@1.0uM		
B-1240	<0.1uM	59.0%@1.0uM		
B-1241	0.04uM	81.0%@1.0uM		
B-1242	0.08uM	83.0%@1.0uM		
B-1243	0.04uM	47.0%@1.0uM		
B-1244	0.26uM	44.0%@1.0uM		
B-1245	0.49uM	42.0%@1.0uM		
B-1246	0.27uM	40.0%@1.0uM		
B-1247	<0.1uM	58.0%@1.0uM		
B-1248	<0.1uM	68.0%@1.0uM		
B-1249	0.24uM	60.0%@1.0uM		
B-1250	0.14uM	18.0%@1.0uM		
B-1251	0.41uM	38.0%@1.0uM		
B-1252	0.17uM	46.0%@1.0uM		
B-1253	0.15uM	57.0%@1.0uM		
B-1254	0.16uM	68.0%@1.0uM		
B-1255	12.9uM	75.0%@1.0uM		
B-1256	0.12uM	41.0%@1.0uM		
B-1257	1.48uM	40.0%@1.0uM		
B-1258	0.07uM	56.0%@1.0uM		
B-1259	<0.1uM	0.48uM		
B-1260	0.11uM	48.0%@1.0uM		
B-1261	0.74uM	44.0%@1.0uM		
B-1262	<0.1uM	63.0%@1.0uM		
B-1263	1.05uM	57.0%@1.0uM		
B-1264	0.32uM	47.0%@1.0uM		
B-1265	0.43uM	51.0%@1.0uM		
B-1266	<0.1uM	58.0%@1.0uM		
B-1267	<0.1uM	73.0%@1.0uM		
B-1268	<0.1uM	79.0%@1.0uM		
B-1269	0.46uM	84.0%@1.0uM		
B-1270	0.47uM	83.0%@1.0uM		
B-1271	0.13uM	74.0%@1.0uM		
B-1272	0.014uM	38.0%@1.0uM		
B-1273	<0.1uM	36.0%@1.0uM		
B-1274	<0.1uM	41.0%@1.0uM		
B-1275	<0.1uM	50.0%@1.0uM		
B-1276	0.062uM	11.0%@1.0uM		
B-1277	<0.1uM	47.0%@1.0uM		
B-1278	0.12uM	85.0%@1.0uM		
B-1279	<0.1uM	79.0%@1.0uM		
B-1280	0.039uM	83.0%@1.0uM		
B-1281	<0.1uM	85.0%@1.0uM		
B-1282	<0.1uM	75.0%@1.0uM		
B-1283	<0.1uM	64.0%@1.0uM		
B-1284	<0.1uM	75.0%@1.0uM		

SUBSTITUTE SHEET (RULE 28)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1285	0.057uM	80.0%@1.0uM		
B-1286	0.15uM	78.0%@1.0uM		
B-1287	0.25uM	55.0%@1.0uM		
B-1288	0.15uM	74.0%@1.0uM		
B-1289	0.73uM	35.0%@1.0uM		
B-1290	0.26uM	75.0%@1.0uM		
B-1291	0.097uM	55.0%@1.0uM		
B-1292	0.01uM	74.0%@1.0uM		
B-1293	0.31uM	48.0%@1.0uM		
B-1294	0.013uM	54.0%@1.0uM		
B-1295	0.079uM	74.0%@1.0uM		
B-1296	0.038uM	48.0%@1.0uM		
B-1297	0.02uM	>1.0uM		
B-1298	0.055uM	20.0%@1.0uM		
B-1299	0.091uM	>1.0uM		
B-1300	0.071uM	18.0%@1.0uM		
B-1301	0.12uM	15.0%@1.0uM		
B-1302	0.023uM	11.0%@1.0uM		
B-1303	0.08uM	>1.0uM		
B-1304	0.11uM	10.0%@1.0uM		
B-1305	0.64uM	9.0%@1.0uM		
B-1306	0.11uM	>1.0uM		
B-1307	0.009uM	16.0%@1.0uM		
B-1308	<0.1uM	>1.0uM		
B-1309	0.045uM	>1.0uM		
B-1310	0.12uM	11.0%@1.0uM		
B-1311	0.05uM	57.0%@1.0uM		
B-1312	0.35uM	>1.0uM		
B-1313	0.035uM	37.0%@1.0uM		
B-1314	0.045uM	24.0%@1.0uM		
B-1315	0.055uM	12.0%@1.0uM		
B-1316	0.026uM	36.0%@1.0uM		
B-1317	0.019uM	9.0%@1.0uM		
B-1318	<0.1uM	1.0%@1.0uM		
B-1319	0.24uM	>1.0uM		
B-1320	0.047uM	43.0%@1.0uM		
B-1321	0.47uM	66.0%@1.0uM		
B-1322	0.12uM	87.0%@1.0uM		
B-1323	0.013uM	85.0%@1.0uM		
B-1324	0.16uM	83.0%@1.0uM		
B-1325	0.27uM	95.0%@1.0uM		
B-1326	0.092uM	84.0%@1.0uM		
B-1327	0.13uM	65.0%@1.0uM		
B-1328	0.032uM	86.0%@1.0uM		
B-1329	0.66uM	54.0%@1.0uM		
B-1330	0.053uM	85.0%@1.0uM		
B-1331	0.004uM	85.0%@1.0uM		
B-1332	0.007uM	81.0%@1.0uM		
B-1333	0.45uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % .. inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1334	0.13uM	73.0%@1.0uM		
B-1335	0.097uM	63.0%@1.0uM		
B-1336	0.072uM	83.0%@1.0uM		
B-1337	0.4uM	90.0%@1.0uM		
B-1338	0.18uM	73.0%@1.0uM		
B-1339	0.12uM	67.0%@1.0uM		
B-1340	0.043uM	63.0%@1.0uM		
B-1341	0.42uM	52.0%@1.0uM		
B-1342	0.25uM	59.0%@1.0uM		
B-1343	0.065uM	83.0%@1.0uM		
B-1344	0.014uM	86.0%@1.0uM		
B-1345	0.27uM	73.0%@1.0uM		
B-1346	0.043uM	86.0%@1.0uM		
B-1347	0.021uM	84.0%@1.0uM		
B-1348	0.009uM	69.0%@1.0uM		
B-1349	0.037uM	86.0%@1.0uM		
B-1350	0.019uM	78.0%@1.0uM		
B-1351	0.068uM	78.0%@1.0uM		
B-1352	0.013uM	76.0%@1.0uM		
B-1353	0.062uM	80.0%@1.0uM		
B-1354	0.013uM	83.0%@1.0uM		
B-1355	0.07uM	75.0%@1.0uM		
B-1356	0.059uM	91.0%@1.0uM		
B-1357	0.18uM	84.0%@1.0uM		
B-1358	0.16uM	76.0%@1.0uM		
B-1359	0.005	84.0%@1.0uM		
B-1360	0.11	0.15uM		54%@3mpk@-4h
B-1361	0.03	0.29uM		
B-1362	0.003	0.29uM		
B-1363	0.009	0.28uM	51.0%@30pmk @- 6H	53%@3mpk@-4h
B-1364	0.009	0.27uM	53.0%@30mpk@- 6.H	17%@3mpk@-4h
B-1365	0.17	88.0%@1.0uM		
B-1366	0.04	0.27uM		
B-1367	<0.1	0.22uM		
B-1368	0.031	0.33uM	44.0%@30mpk @-	
B-1369	<0.1	0.29uM		
B-1370	<0.1	0.77uM		
B-1371	0.06	83.0%@1.0uM		
B-1372	<0.1	0.41uM	48.0%@30mpk @-	
B-1373	0.016	0.17uM		
B-1374	<0.1	0.28uM		
B-1375	0.01	0.25uM		
B-1376	0.009	0.26uM	3.0%@30mpk @-6H	
B-1377	0.12	5.0uM		
B-1378	0.02	1.04uM		
B-1379	<0.1	0.092uM		
B-1380	<0.1	0.26uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1381	0.055	0.73uM		
B-1382	<0.1	0.44uM		
B-1383	0.0012	0.15uM		
B-1384	0.57	0.37uM		
B-1385	<0.1	0.11uM		
B-1386	<0.1	0.25uM		
B-1387	<0.1	0.1uM		
B-1388	0.57	1.38uM		
B-1389	0.06	0.57uM		
B-1390	<0.1	71.0%@1.0uM		
B-1391	0.016uM	82.0%@1.0uM		
B-1392	0.059uM	82.0%@1.0uM		
B-1393	3.17uM	80.0%@1.0uM		
B-1394	0.32uM	78.0%@1.0uM		
B-1395	1.48	61.0%@1.0uM		
B-1396	1.55	73.0%@1.0uM		
B-1397	0.92	85.0%@1.0uM		
B-1398	0.67	83.0%@1.0uM		
B-1399	0.14	74.0%@1.0uM		
B-1400	0.024	83.0%@1.0uM		
B-1401	0.033	75.0%@1.0uM		
B-1402	0.12	76.0%@1.0uM		
B-1403	4.54	71%@1.0uM		
B-1404	0.6	70%@1.0uM		
B-1405	0.28	70%@1.0uM		
B-1406	1.39	56.0%@1.0uM		
B-1407	0.4	71.0%@1.0uM		
B-1408	0.27	69.0%@1.0uM		
B-1409	<0.1	72.0%@1.0uM		
B-1410	<0.1	69%@1.0uM		
B-1411	<0.1	81.0%@1.0uM		
B-1412	0.097	80.0%@1.0uM		
B-1413	0.016	78.0%@1.0uM		
B-1414	0.025	83.0%@1.0uM		
B-1415	1.41	79.0%@1.0uM		
B-1416	0.14	81.0%@1.0uM		
B-1417	0.069	69.0%@1.0uM		
B-1418	1.01	82.0%@1.0uM		
B-1419	0.3	84.0%@1.0uM		
B-1420	<0.1	82.0%@1.0uM		
B-1421	0.014	75.0%@1.0uM		
B-1422	0.58	68.0%@1.0uM		
B-1423	1.58	84.0%@1.0uM		
B-1424	0.86	76.0%@1.0uM		
B-1425	0.09	83.0%@1.0uM		
B-1426	0.19	80.0%@1.0uM		
B-1427	<0.1	84.0%@1.0uM		
B-1428	<0.1	86.0%@1.0uM		
B-1429	<0.1	87.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1430	0.75uM	35.0% @ 1.0uM		
B-1431	0.36uM	58.0% @ 1.0uM		
B-1432	0.11uM	51.0% @ 1.0uM		
B-1433	0.26uM	21.0% @ 1.0uM		
B-1434	0.19uM	28.0% @ 1.0uM		
B-1435	1.8uM	45.0% @ 1.0uM		
B-1436	1.0uM	20.0% @ 1.0uM		
B-1437	0.3uM	23.0% @ 1.0uM		
B-1438	2.01uM	27.0% @ 1.0uM		
B-1439	1.7uM	17.0% @ 1.0uM		
B-1440	0.87uM	3.0% @ 1.0uM		
B-1441	1.95uM	66.0% @ 1.0uM		
B-1442	1.54uM	18.0% @ 1.0uM		
B-1443	0.014uM	83.0% @ 1.0uM		
B-1444	0.3uM	24.0% @ 1.0uM		
B-1445	0.43uM	27.0% @ 1.0uM		
B-1446	0.77uM	36.0% @ 1.0uM		
B-1447	0.5uM	34.0% @ 1.0uM		
B-1448	1.43uM	22.0% @ 1.0uM		
B-1449	1.61uM	50.0% @ 1.0uM		
B-1450	2.1uM	49.0% @ 1.0uM		
B-1451	2.88uM	50% @ 1.0uM		
B-1452	2.41uM	47.0% @ 1.0uM		
B-1453	2.53uM	49.0% @ 1.0uM		
B-1454	1.6uM	12.0% @ 1.0uM		
B-1455	1.21uM	8.0% @ 1.0uM		
B-1456	1.29uM	>1.0uM		
B-1457	0.43uM	43.0% @ 1.0uM		
B-1458	0.95uM	65.0% @ 1.0uM		
B-1459	0.67uM	46.0% @ 1.0uM		
B-1460	0.96uM	29.0% @ 1.0uM		
B-1461	0.4uM	39.0% @ 1.0uM		
B-1462	0.22uM	50.0% @ 1.0uM		
B-1463	2.34uM	26.0% @ 1.0uM		
B-1464	1.18uM	27.0% @ 1.0uM		
B-1465	3.23uM	31.0% @ 1.0uM		
B-1466	1.69uM	>1.0uM		
B-1467	1.22uM	1.0% @ 1.0uM		
B-1468	1.61uM	10.0% @ 1.0uM		
B-1469	0.37uM	14.0% @ 1.0uM		
B-1470	0.6uM	28.0% @ 1.0uM		
B-1471	0.85uM	25.0% @ 1.0uM		
B-1472	0.93uM	12.0% @ 1.0uM		
B-1473	1.24uM	14.0% @ 1.0uM		
B-1474	1.23uM	31.0% @ 1.0uM		
B-1475	2.1uM	24.0% @ 1.0uM		
B-1476	0.047uM	42.0% @ 1.0uM		
B-1477	2.5uM	34.0% @ 1.0uM		
B-1478				

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Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1479				

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2270	0.72uM	31%@10.0uM		
B-2271	0.93uM	38%@10.0uM		
B-2272	0.26uM	53.0%@10.0uM		
B-2273	1.92uM	39.0%@10.0uM		
B-2274	0.26uM	59.0%@10.0uM		
B-2275	2.16uM	53.0%@10.0uM		
B-2276	11.5uM	37.0%@10.0uM		
B-2277	14.9uM	44.0%@10.0uM		
B-2278	0.8uM	51.0%@10.0uM		
B-2279	0.32uM	36.0%@10.0uM		
B-2280	0.4uM	57.0%@10.0uM		
B-2281	0.81uM	60.0%@10.0uM		
B-2282	0.91uM	41.0%@10.0uM		
B-2283	0.04uM	53.0%@10.0uM		
B-2284	4.61uM	62.0%@10.0uM		
B-2285	2.29uM	49.0%@10.0uM		
B-2286	0.017uM	0.78uM	25%@30mpk@-1h	
B-2287	2.56uM	61.0%@10.0uM		
B-2288	6.51uM	46.0%@10.0uM		
B-2289	3.0uM	30.0%@10.0uM		
B-2290	2.37uM	59.0%@10.0uM		
B-2291	0.019uM	41%@10.0uM		
B-2292	8.82uM	57.0%@10.0uM		
B-2293	2.11uM	56.0%@10.0uM		
B-2294	1.68uM	50.0%@10.0uM		
B-2295	1.79uM	56.0%@10.0uM		
B-2296	17.3uM	63.0%@10.0uM		
B-2297	3.59uM	57.0%@10.0uM		
B-2298	0.29uM	4.22uM		
B-2299	1.97uM	62.0%@10.0uM		
B-2300	0.07uM	43.0%@10.0uM		
B-2301	0.18uM	44.0%@10.0uM		
B-2302	1.0uM	58.0%@1.0uM		
B-2303	0.011uM	54.0%@10.0uM		
B-2304	1.41uM	50.0%@10.0uM		
B-2305	0.54uM	60.0%@10.0uM		
B-2306	5.88uM	39.0%@10.0uM		
B-2307	2.29uM	69.0%@10.0uM		
B-2308	0.66uM	56.0%@10.0uM		
B-2309	0.29uM	47.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2310	0.12uM	1.2uM	50% @ 30mpk @ -6h	
B-2311	7.18uM	60% @ 10.0uM		
B-2312	2.93uM	43.0% @ 10.0uM		
B-2313	42.3uM	58.0% @ 10.0uM		
B-2314	11.0uM	66.0% @ 10.0uM		
B-2315	0.49uM	36.0% @ 10.0uM		
B-2316	0.46uM	58.0% @ 10.0uM		
B-2317	1.0uM	60.0% @ 10.0uM		
B-2318	73.0% @ 10.0uM	25.0% @ 10.0uM		
B-2319	75.0% @ 10.0uM	40.0% @ 10.0uM		
B-2320	44.0% @ 10.0uM	35.0% @ 10.0uM		
B-2321	69.0% @ 10.0uM	27.0% @ 10.0uM		
B-2322	76.0% @ 10.0uM	38.0% @ 10.0uM		
B-2323	69.0% @ 10.0uM	46.0% @ 10.0uM		
B-2324	58.0% @ 10.0uM	36.0% @ 10.0uM		
B-2325	60.0% @ 10.0uM	51.0% @ 10.0uM		
B-2326	76.0% @ 10.0uM	33.0% @ 10.0uM		
B-2327	76.0% @ 10.0uM	23.0% @ 10.0uM		
B-2328	65.0% @ 10.0uM	28.0% @ 10.0uM		
B-2329	72.0% @ 10.0uM	53.0% @ 10.0uM		
B-2330	81.0% @ 10.0uM	37.0% @ 10.0uM		
B-2331	74.0% @ 10.0uM	44.0% @ 10.0uM		
B-2332	70.0% @ 10.0uM	47.0% @ 10.0uM		
B-2333	58.0% @ 10.0uM	36.0% @ 10.0uM		
B-2334	81.0% @ 10.0uM	45.0% @ 10.0uM		
B-2335	82.0% @ 10.0uM	50.0% @ 10.0uM		
B-2336	48.0% @ 10.0uM	35.0% @ 10.0uM		
B-2337	46.0% @ 10.0uM	59.0% @ 10.0uM		
B-2338	73.0% @ 10.0uM	50.0% @ 10.0uM		
B-2339	84.0% @ 10.0uM	>10.0uM		
B-2340	35.0% @ 10.0uM	12.0% @ 10.0uM		
B-2341	75.0% @ 10.0uM	50.0% @ 10.0uM		
B-2342	83.0% @ 10.0uM	46.0% @ 10.0uM		
B-2343	43.0% @ 10.0uM	27.0% @ 10.0uM		
B-2344	71.0% @ 10.0uM	50.0% @ 10.0uM		
B-2345	64.0% @ 10.0uM	38.0% @ 10.0uM		
B-2346	45.0% @ 10.0uM	48.0% @ 10.0uM		
B-2347	49.0% @ 10.0uM	50.0% @ 10.0uM		
B-2348	76.0% @ 10.0uM	48.0% @ 10.0uM		
B-2349	75.0% @ 10.0uM	27.0% @ 10.0uM		

SUBSTITUTE SHEET (RULE 26)

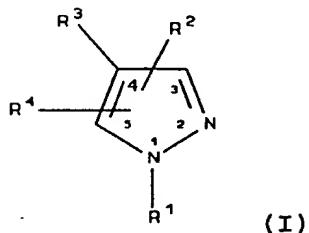
Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2350	38.0% @ 10.0uM	56.0% @ 10.0uM		
B-2351	77.0% @ 10.0uM	1.0% @ 10.0uM		
B-2352	37.0% @ 10.0uM	19.0% @ 10.0uM		
B-2353	38.0% @ 10.0uM	33.0% @ 10.0uM		
B-2354	65.0% @ 10.0uM	25.0% @ 10.0uM		
B-2355	84.0% @ 10.0uM	50.0% @ 10.0uM		
B-2356	77.0% @ 10.0uM	45.0% @ 10.0uM		
B-2357	47.0% @ 10.0uM	41.0% @ 10.0uM		
B-2358	17.0% @ 10.0uM	52.0% @ 10.0uM		
B-2359	76.0% @ 10.0uM	35.0% @ 10.0uM		
B-2360	45.0% @ 10.0uM	>10.0uM		
B-2361	19.0% @ 10.0uM	46.0% @ 10.0uM		
B-2362	60% @ 100.0uM	39.0% @ 10.0uM		
B-2363	44.0% @ 10.0uM	1.0% @ 10.0uM		
B-2364	47.0% @ 10.0uM	4.0% @ 10.0uM		
B-2365	82.0% @ 10.0uM	43.0% @ 10.0uM		
B-2366	70.0% @ 10.0uM	59.0% @ 10.0uM		
B-2367	46.0% @ 10.0uM	40.0% @ 1.0uM		
B-2368	65.0% @ 10.0uM	55.0% @ 10.0uM		
B-2369	32.0% @ 10.0uM	>10.0uM		
B-2370	73% @ 100.0uM	20.0% @ 10.0uM		
B-2371	54.0% @ 10.0uM	36.0% @ 10.0uM		
B-2372	55.0% @ 100.0uM	>10.0uM		
B-2373	50.0% @ 100.0uM	6% @ 10.0uM		
B-2374	35.0% @ 10.0uM	20.0% @ 10.0uM		
B-2375	62.0% @ 100.0uM	>10.0uM		
B-2376	32.0% @ 10.0uM	17.0% @ 10.0uM		
B-2377	34.0% @ 10.0uM	17.0% @ 10.0uM		
B-2378	48.0% @ 10.0uM	61.0% @ 10.0uM		
B-2379	73.0% @ 100.0uM	45.0% @ 1.0uM		
B-2380	81% @ 100.0uM	53.0% @ 10.0uM		
B-2381	68% @ 100.0uM	2.0% @ 10.0uM		
B-2382	51.0% @ 10.0uM	24.0% @ 10.0uM		
B-2383	63.0% @ 10.0uM	35.0% @ 10.0uM		
B-2384	49% @ 100.0uM	10.0% @ 10.0uM		
B-2385	79.0% @ 10.0uM	19.0% @ 10.0uM		
B-2386	38.0% @ 10.0uM	19.0% @ 10.0uM		
B-2387	50.0% @ 100.0uM	>10.0uM		
B-2388	42.0% @ 10.0uM	24.0% @ 10.0uM		
B-2389	39.0% @ 10.0uM	29.0% @ 10.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2390	34.0%@10.0uM	27.0%@1.0uM		
B-2391	40.0%@10.0uM	59.0%@10.0uM		
B-2392	63.0%@10.0uM	46.0%@10.0uM		
B-2393	43.0%@10.0uM	>10.0uM		
B-2394	37.0%@10.0uM	22.0%@10.0uM		
B-2395	32.0%@10.0uM	28.0%@10.0uM		
B-2396	75.0%@10.0uM	>10.0uM		
B-2397	83.0%@10.0uM	22.0%@10.0uM		
B-2398	55%@100.0uM	10.0%@10.0uM		
B-2399	69.0%@10.0uM	18.0%@10.0uM		
B-2400	60.0%@10.0uM	40.0%@10.0uM		
B-2401	78.0%@10.0uM	44.0%@10.0uM		
B-2402	43.0%@10.0uM	52.0%@10.0uM		
B-2403	72%@100.0uM	52.0%@10.0uM		
B-2404	58%@100.0uM	52.0%@10.0uM		
B-2405	47%@100.0uM	>10.0uM		
B-2406	45.0%@10.0uM	24.0%@10.0uM		
B-2407	47%@100.0uM	27.0%@10.0uM		
B-2408	39.0%@10.0uM	10.0%@10.0uM		
B-2409	78.0%@10.0uM	26.0%@10.0uM		
B-2410	33.0%@10.0uM	32.0%@10.0uM		
B-2411	26%@100.0uM	13.0%@10.0uM		
B-2412	40.0%@10.0uM	31.0%@10.0uM		
B-2413	75.0%@10.0uM	37.0%@10.0uM		
B-2414	86.0%@10.0uM	38.0%@10.0uM		
B-2415	94.0%@10.0uM	50.0%@10.0uM		
B-2416	85.0%@10.0uM	43.0%@1.0uM		
B-2417	83.0%@10.0uM	18.0%@10.0uM		
B-2418	88.0%@10.0uM	34.0%@10.0uM		
B-2419	86.0%@10.0uM	66.0%@10.0uM		
B-2420	70.0%@10.0uM	34.0%@10.0uM		
B-2421	89.0%@10.0uM	38.0%@10.0uM		
B-2422	90.0%@10.0uM	17.0%@10.0uM		
B-2423	85.0%@10.0uM	>10.0uM		
B-2424	86.0%@10.0uM	43.0%@10.0uM		
B-2425	79.0%@10.0uM	42.0%@10.0uM		
B-2426	88.0%@10.0uM	53.0%@10.0uM		
B-2427	87.0%@10.0uM	59.0%@10.0uM		
B-2428	82.0%@10.0uM	50.0%@10.0uM		
B-2429	92.0%@10.0uM	32.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2430	90.0%@10.0uM	61.0%@10.0uM		
B-2431	85.0%@10.0uM	68.0%@10.0uM		
B-2432	86.0%@10.0uM	40.0%@10.0uM		
B-2433	94.0%@10.0uM	84.0%@10.0uM		
B-2434	92.0%@10.0uM	63.0%@10.0uM		
B-2435	84.0%@10.0uM	4.0%@10.0uM		
B-2436	80.0%@10.0uM	54.0%@10.0uM		
B-2437	82.0%@10.0uM	41.0%@10.0uM		
B-2438	75.0%@10.0uM	40.0%@10.0uM		
B-2439	81.0%@10.0uM	44.0%@10.0uM		
B-2440	77.0%@10.0uM	78.0%@10.0uM		
B-2441	86.0%@10.0uM	46.0%@10.0uM		
B-2442	86.0%@10.0uM	>10.0uM		
B-2443	84.0%@10.0uM	44.0%@10.0uM		
B-2444	89.0%@10.0uM	7.0%@10.0uM		
B-2445	94.0%@10.0uM	15.0%@10.0uM		
B-2446	90.0%@10.0uM	28.0%@10.0uM		
B-2447	94.0%@10.0uM	>10.0uM		
B-2448	75.0%@10.0uM	30.0%@10.0uM		
B-2449	86.0%@10.0uM	42.0%@10.0uM		
B-2450	87.0%@10.0uM	46.0%@1.0uM		
B-2451	87.0%@10.0uM	45.0%@10.0uM		
B-2452	89.0%@10.0uM	33.0%@10.0uM		
B-2453	91.0%@10.0uM	>10.0uM		
B-2454	88.0%@10.0uM	40.0%@10.0uM		
B-2455	87.0%@10.0uM	54.0%@10.0uM		
B-2456	86.0%@10.0uM	53.0%@10.0uM		
B-2457	90.0%@10.0uM	18.0%@10.0uM		
B-2458	83.0%@10.0uM	36.0%@10.0uM		
B-2459	82.0%@10.0uM	81.0%@10.0uM		
B-2460	80.0%@10.0uM	79.0%@10.0uM		
B-2461	67.0%@10.0uM	59.0%@10.0uM		

WHAT WE CLAIM IS:

1. A compound of Formula I



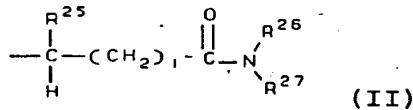
5 wherein

R¹ is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, 10 haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, 15 alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, 20 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxy carbonylalkylene, aryloxycarbonylalkylene, heterocyclyloxycarbonylalkylene, 25 arylcarbonylalkylene, heterocyclycarbonylalkylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclycarbonylalkylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, 30 heterocyclycarbonyloxyalkylene, alkylcarbonyloxyarylene,

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arylcarbonyloxyarylene, and
heterocyclcarbonyloxyarylene; or

R¹ has the formula



35 wherein:

i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl,
heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,

40 alkylcarbonylalkylene, arylcarbonylalkylene, and
heterocyclcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl,
alkynyl, cycloalkylalkylene, aralkyl,
alkoxycarbonylalkylene, and alkylaminoalkyl; and

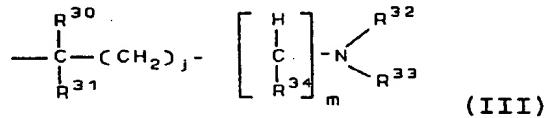
45 R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
aryl, heterocycl, aralkyl, cycloalkylalkylene,
cycloalkenylalkylene, cycloalkylarylene,
cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene,
alkylaralkyl, aralkylarylene, alkylheterocycl,
50 alkylheterocyclalkylene, alkylheterocyclarylene,
aralkylheterocycl, alkoxyalkylene, alkoxyarylene,
alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene,
aryloxyarylene, aralkoxyarylene,
alkoxyheterocyclalkylene, aryloxyalkoxyarylene,
55 alkoxy carbonylalkylene, alkoxy carbonyl heterocycl,
alkoxy carbonyl heterocycl carbonyl alkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
arylamino carbonylalkylene, alkylaminocarbonylalkylene,
60 arylcarbonylalkylene, alkoxy carbonylarylene,
aryloxy carbonylarylene, alkylaryloxy carbonylarylene,
arylcarbonylarylene, alkylarylcarbonylarylene,

alkoxycarbonylheterocyclarylene,
alkoxycarbonylalkoxylarylene,
65 heterocyclcarbonylalkylarylene, alkylthioalkylene,
cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
70 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
heterocyclalkylene, alkylheterocyclarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclthioarylene,
75 arylthioalkylarylene, and alkylsulfonylarylene groups
are optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or
R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹
80 is selected from aralkyl, aralkoxyalkylene,
heterocyclalkylene, alkylheterocyclalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocycl groups are optionally substituted with one
85 or more radicals independently selected from alkyl and
nitro; or
R²⁶ and R²⁷ together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
90 radicals independently selected from alkyl, aryl,
heterocyclyl, heterocyclalkylene,
alkylheterocyclalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
95 alkoxycarbonylamino; wherein said aryl,
heterocyclalkylene and aryloxyalkylene radicals are
optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;

and

100 R² is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocycllamino, heterocyclalkylamino, aralkylamino, 105 aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocyclxyoxy, alkylthio, arylthio, heterocyclthio, carboxy, carboxyalkyl, 110 carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylheterocycl, alkoxycarbonylheterocyclcarbonyl, alkoxyalkylamino, alkoxycarbonylaminoalkylamino, and heterocyclsulfonyl; 115 wherein the aryl, heterocyclyl, heterocyclalkyl, cycloalkyl and cycloalkenyl groups are optionally substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclalkyl, epoxalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, arylsulfonyl, and aralkylsulfonyl; or

120 R² has the formula:



wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

130 R³⁰ and R³¹ are independently selected from hydrogen,

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alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

- R³² is selected from hydrogen, alkyl, aralkyl,
 135 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

- R³³ is selected from hydrogen, alkyl, -C(O)R³⁵,
 140 -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵, R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

- R³⁴ is selected from hydrogen, alkyl, aminocarbonyl,
 145 alkylaminocarbonyl, and arylaminocarbonyl; or
 R² is -CR⁴¹R⁴² wherein R⁴¹ is aryl, and R⁴² is hydroxy; and
 R³ is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



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(IV)

(V)

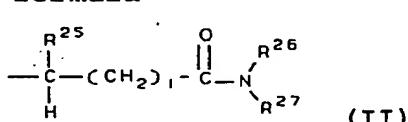
wherein R⁴³ is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

- wherein the R³ pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclalkoxy, amino, alkylamino,
 155
 160

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alkenylamino, alkynylamino, cycloalkylamino,
cycloalkenylamino, arylamino, heterocyclylamino,
aminocarbonyl, cyano, hydroxy, hydroxyalkyl,
alkoxycarbonyl, aryloxycarbonyl, heterocyclloxycarbonyl,
165 alkoxy carbonylamino, alkoxyaralkylamino, aminosulfinyl,
aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino,
aralkylamino, heterocyclalkylamino,
aralkylheterocyclamino, nitro, alkylaminocarbonyl,
alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl,
170 alkylcarbonyl, hydrazinyl, alkylhydrazinyl,
arylhydrazinyl, or -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or
amino, and R⁴⁵ is alkyl or aralkyl; and
R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,
175 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
R⁴ is optionally substituted with one or more radicals
independently selected from halo, alkyl, alkenyl,
alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
alkylsulfinylalkylene, arylsulfinylalkylene,
180 alkylsulfonyl, alkylsulfonylalkylene,
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
185 arylaminoalkylene, aminoalkylamino, and hydroxy;
provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring
containing a 2-hydroxy substituent and when R¹ is hydrido;
further provided R² is selected from aryl, heterocyclyl,
unsubstituted cycloalkyl and cycloalkenyl when R⁴ is
190 hydrido; and further provided R⁴ is not
methylsulfonylphenyl; or
a pharmaceutically-acceptable salt or tautomer
thereof.

2. A compound of Claim 1 wherein
 R¹ is selected from hydrido, lower alkyl, lower
 cycloalkyl, lower alkenyl, lower alkynyl, lower
 heterocyclyl, lower cycloalkylalkylene, lower haloalkyl,
 5 lower hydroxyalkyl, lower aralkyl, lower alkoxyalkyl,
 lower mercaptoalkyl, lower alkylthioalkylene, amino,
 lower alkylamino, lower arylamino, lower
 alkylaminoalkylene, and lower heterocyclylalkylene; or
 R¹ has the formula



wherein:

i is 0, 1 or 2; and

R²⁵ is selected from hydrogen, lower alkyl, lower phenylalkyl, lower heterocyclylalkyl, lower 15 alkoxyalkylene, lower phenoxyalkylene, lower aminoalkyl, lower alkylaminoalkyl, lower phenoxyaminoalkyl, lower alkylcarbonylalkylene, lower phenoxy carbonylalkylene, and lower heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, lower alkyl, lower 20 alkenyl, lower alkynyl, lower cycloalkylalkylene, lower phenylalkyl, lower alkoxy carbonylalkylene, and lower alkylaminoalkyl; and

R²⁷ is selected from lower alkyl, lower cycloalkyl, lower alkynyl, aryl selected from phenyl, biphenyl and 25 naphthyl, lower heterocyclyl, lower phenylalkyl, lower cycloalkylalkylene, lower cycloalkenylalkylene, lower cycloalkylarylene, lower cycloalkylcycloalkyl, lower heterocyclylalkylene, lower alkylphenylene, lower alkylphenylalkyl, lower phenylalkylphenylene, lower 30 alkylheterocyclyl, lower alkylheterocyclylalkylene, lower alkylheterocyclylphenylene, lower

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phenylalkylheterocyclyl, lower alkoxyalkylene, lower
alkoxyphenylene, lower alkoxyphenylalkyl, lower
alkoxyheterocyclyl, lower alkoxyalkoxyphenylene, lower
35 phenoxyphenylene, lower phenylalkoxyphenylene, lower
alkoxyheterocyclalkylene, lower phenoxyalkoxyphenylene,
lower alkoxycarbonylalkylene, lower
alkoxycarbonylheterocyclyl, lower
alkoxycarbonylheterocyclcarbonylalkylene, lower
40 aminoalkyl, lower alkylaminoalkylene, lower
phenylaminocarbonylalkylene, lower
alkoxyphenylaminocarbonylalkylene, lower
aminocarbonylalkylene, arylaminocarbonylalkylene, lower
alkylaminocarbonylalkylene, lower phenylcarbonylalkylene,
45 lower alkoxycarbonylphenylene, lower
phenoxy carbonylphenylene, lower
alkylphenoxy carbonylphenylene, lower
phenylcarbonylphenylene, lower
alkylphenylcarbonylphenylene, lower
50 alkoxy carbonylheterocyclphenylene, lower
alkoxy carbonylalkoxyphenylene, lower
heterocyclcarbonylalkylphenylene, lower
alkylthioalkylene, cycloalkylthioalkylene, lower
alkylthiophenylene, lower phenylalkylthiophenylene, lower
55 heterocyclthiophenylene, lower
phenylthioalkylphenylene, lower
phenylsulfonylaminoalkylene, lower
alkylsulfonylphenylene, lower
alkylaminosulfonylphenylene; wherein said lower alkyl,
60 lower cycloalkyl, aryl selected from phenyl, biphenyl and
naphthyl, lower heterocyclyl, lower phenylalkyl, lower
heterocyclalkylene, lower alkylheterocyclphenylene,
lower alkoxyphenylene, lower phenoxyphenylene, lower
phenylaminocarbonylalkylene, lower
65 phenoxy carbonylphenylene, lower phenylcarbonylphenylene,
lower alkylthiophenylene, lower
heterocyclthiophenylene, lower

phenylthioalkylphenylene, and lower alkylsulfonylphenylene groups are optionally substituted with one or more radicals independently selected from lower alkyl, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, and cyano; or

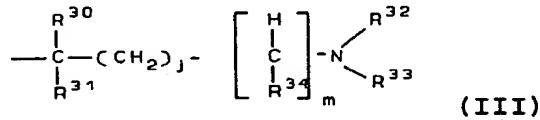
R²⁷ is -CHR⁴⁶R⁴⁷ wherein R⁴⁶ is lower alkoxycarbonyl, and R⁴⁷ is selected from lower phenylalkyl, lower phenylalkoxyalkylene, lower heterocyclalkylene, lower alkylheterocyclalkylene, lower alkylthioalkylene, and lower phenylalkylthioalkylene; wherein said phenylalkyl and heterocyclyl groups are optionally substituted with one or more radicals independently selected from lower alkyl and nitro; or

R²⁶ and R²⁷ together with the nitrogen atom to which they are attached form a 4-8 membered ring heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from lower alkyl, aryl selected from phenyl, biphenyl and naphthyl, heterocyclyl, heterocyclalkylene, lower alkylheterocyclalkylene, lower phenoxyalkylene, lower alkoxyphenylene, lower alkylphenoxyalkylene, lower alkylcarbonyl, lower alkoxycarbonyl, lower phenylalkoxycarbonyl, lower alkylamino and lower alkoxycarbonylamino; wherein said aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclalkylene and lower phenoxyalkylene radicals are optionally substituted with one or more radicals independently selected from halogen, lower alkyl and lower alkoxy; and

R² is selected from hydrido, halogen, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, lower haloalkyl, lower hydroxyalkyl, 5- or 6-membered heterocyclyl, lower alkylheterocyclyl, lower heterocyclalkyl, lower alkylamino, lower alkynylamino, phenylamino, lower heterocyclamino, lower heterocyclalkylamino, lower phenylalkylamino, lower

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- aminoalkyl, lower aminoalkylamino, lower
 105 alkylaminoalkylamino, lower cycloalkyl, lower alkenyl,
 lower alkoxy carbonylalkyl, lower cycloalkenyl, lower
 carboxyalkylamino, lower alkoxy carbonyl, lower
 heterocyclyl carbonyl, lower alkoxy carbonyl heterocyclyl,
 lower alkoxy carbonyl heterocyclyl carbonyl,
 110 alkoxy carbonylalkyl, lower alkoxyalkylamino, lower
 alkoxy carbonylaminoalkylamino, lower
 heterocyclylsulfonyl, lower heterocyclyloxy, and lower
 heterocyclylthio; wherein the aryl, heterocyclyl,
 heterocyclylalkyl, cycloalkyl, and cycloalkenyl groups
 115 are optionally substituted with one or more radicals
 independently selected from halo, keto, lower alkyl,
 lower alkynyl, phenyl, 5- or 6-membered heterocyclyl,
 lower phenylalkyl, lower heterocyclylalkyl, lower
 epoxyalkyl, carboxy, lower alkoxy, lower aryloxy, lower
 120 phenylalkoxy, lower haloalkyl, lower alkylamino, lower
 alkylaminoalkylamino, lower alkynylamino, lower
 amino(hydroxyalkyl), lower heterocyclylalkylamino, lower
 alkylcarbonyl, lower alkoxy carbonyl, lower alkylsulfonyl,
 lower phenylalkylsulfonyl, and phenylsulfonyl; or
 125 R² has the formula:



wherein:

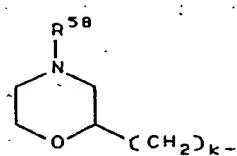
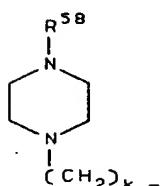
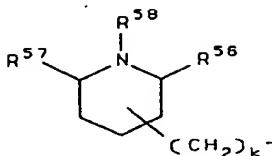
- j is 0, 1 or 2; and
 m is 0;
 130 R³⁰ and R³¹ are independently selected from hydrogen,
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,
 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and
 R³² is selected from hydrogen, alkyl, aralkyl,
 135 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,

SUBSTITUTE SHEET (RULE 26)

aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
alkylcarbonylalkylene, arylcarbonylalkylene, and
heterocyclcarbonylaminoalkylene; and
R³³ is selected from hydrogen, alkyl, -C(O)R³⁵,
140 -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰;
wherein R³⁵ is selected from alkyl, cycloalkyl,
haloalkyl, alkenyl, aryl, heterocycl, aralkyl,
arylcycloalkyl, cycloalkenylalkylene,
heterocyclalkylene, alkylarylene, alkylheterocycl,
145 arylarylene, arylheterocycl, alkoxy, alkenoxy,
alkoxyalkylene, alkoxyaralkyl, alkoxyarylene,
aryloxyalkylene, aralkoxyalkylene, cycloalkyloxyalkylene,
alkoxycarbonyl, heterocyclcarbonyl,
alkylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
150 alkoxy carbonylalkylene, alkoxy carbonylarylene,
aralkoxy carbonylheterocycl, alkylcarbonylheterocycl,
arylcarbonyloxyalkylarylene, and alkylthioalkylene;
wherein said aryl, heterocycl, aralkyl, alkylarylene,
arylheterocycl, alkoxyarylene, aryloxyalkylene,
155 cycloalkoxyalkylene, alkoxy carbonylalkylene, and
alkylcarbonylheterocycl groups are optionally
substituted with one or more radicals independently
selected from alkyl, halo, haloalkyl, alkoxy, haloalkoxy,
keto, amino, nitro, and cyano; or
160 R³⁵ is CHR⁴⁸R⁴⁹ wherein R⁴⁸ is arylsulfonylamino or
alkylarylsulfonylamino, and R⁴⁹ is selected from aralkyl,
amino, alkylamino, and aralkylamino; or
R³⁵ is -NR⁵⁰R⁵¹ wherein R⁵⁰ is alkyl, and R⁵¹ is aryl;
and
165 wherein R³⁶ is selected from alkyl, haloalkyl, aryl,
heterocycl, cycloalkylalkylene, alkylarylene,
alkenylarylene, arylarylene, aralkyl, aralkenyl,
heterocyclheterocycl, carboxyarylene, alkoxyarylene,
alkoxycarbonylarylene, alkylcarbonylaminoarylene,
170 alkylcarbonylaminoheterocycl,
arylcarbonylaminoalkylheterocycl, alkylaminoarylene,

alkylamino, alkylaminoarylene, alkylsulfonylarylene,
alkylsulfonylaralkyl, and arylsulfonylheterocyclyl;
wherein said aryl, heterocyclyl, cycloalkylalkylene,
175 aralkyl, alkylcarbonylaminotheterocyclyl, and
alkylsulfonylarylene groups are optionally substituted
with one or more radicals independently selected from
alkyl, halo, hydroxy, haloalkyl, alkoxy, haloalkoxy,
keto, amino, nitro, and cyano; and
180 wherein R³⁷ is selected from hydrogen and alkyl; and
wherein R³⁸ is selected from hydrogen, alkyl,
alkenyl, aryl, heterocyclyl, aralkyl, alkylarylene,
arylcloalkyl, arylarylene, cycloalkylalkylene,
heterocyclylalkylene, alkylheterocyclylalkylene,
185 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
aryloxyarylene, arylcarbonyl, alkoxycarbonyl,
alkoxycarbonylalkylene, alkoxycarbonylarylene,
alkylcarbonylcarbonylalkylene, alkylaminoalkylene,
alkylaminoaralkyl, alkylcarbonylaminoalkylene,
190 alkylthioarylene, alkylsulfonylaralkyl, and
aminosulfonylaralkyl; wherein said aryl, heterocyclyl,
aralkyl, and heterocyclylalkylene groups are optionally
substituted with one or more radicals independently
selected from alkyl, halo, hydroxy, haloalkyl, alkoxy,
195 haloalkoxy, keto, amino, nitro, and cyano; or
R³⁸ is -CR⁵²R⁵³ wherein R⁵² is aloxycarbonyl, and R⁵³
is alkylthioalkylene; or
R³⁷ and R³⁸ together with the nitrogen atom to which
they are attached form a heterocycle; and
200 R³⁹ and R⁴⁰ have the same definition as R²⁶ and R²⁷ in
claim 1; or
R² is -CR⁵⁴R⁵⁵ wherein R⁵⁴ is phenyl and R⁵⁵ is hydroxy;
or
R² is selected from the group consisting of

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(VI)

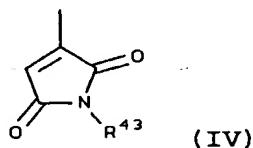
(VII)

(VIII)

wherein

- 210 k is an integer from 0 to 3; and
 R⁵⁶ is hydrogen or lower alkyl; and
 R⁵⁷ is hydrogen or lower alkyl; or
 R⁵⁶ and R⁵⁷ form a lower alkylene bridge; and
 R⁵⁸ is selected from hydrogen, alkyl, aralkyl, aryl,
 heterocyclyl, heterocyclylalkyl, alkoxy carbonyl,
 alkylsulfonyl, aralkylsulfonyl, arylsulfonyl, -C(O)R⁵⁹,
 -SO₂R⁶⁰, and -C(O)NHR⁶¹;
 wherein R⁵⁹ is selected from alkyl, haloalkyl,
 cycloalkyl, aryl, heterocyclyl, alkylarylene, aralkyl,
 alkylheterocyclyl, alkoxy, alkenoxy, aralkoxy,
 alkoxyalkylene, alkoxyarylene, alkoxyaralkyl; wherein
 said aryl, heterocyclyl, and aralkyl groups are
 optionally substituted with one or more radicals
 independently selected from alkyl, halo, hydroxy,
 haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and
 cyano; and
 wherein R⁶⁰ is selected from alkyl, aryl,
 heterocyclyl, alkylarylene, alkylheterocyclyl, aralkyl,
 heterocyclylheterocyclyl, alkoxyarylene, alkylamino,
 alkylaminoarylene, alkylsulfonylarylene, and
 arylsulfonylheterocyclyl; wherein said aryl,
 heterocyclyl, and aralkyl groups are optionally
 substituted with one or more radicals independently
 selected from alkyl, halo, hydroxy, haloalkyl, alkoxy,
 haloalkoxy, keto, amino, nitro, and cyano; and

- wherein R⁶¹ is selected from alkyl, aryl,
 235 alkylarylene, and alkoxyarylene; wherein said aryl group
 is optionally substituted with one or more radicals
 independently selected from alkyl, halo, hydroxy,
 haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and
 cyano; and
 240 R³ is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, and



- wherein R⁴³ is selected from hydrogen, lower alkyl,
 lower aminoalkyl, lower alkoxyalkyl, lower alkenoxyalkyl
 245 and lower aryloxyalkyl; and
 wherein the R³ pyridinyl, pyrimidinyl, quinolinyl and
 purinyl groups are optionally substituted with one or
 more radicals independently selected from lower
 alkylthio, lower alkylsulfonyl, aminosulfonyl, halo,
 250 lower alkyl, lower aralkyl, lower phenylalkenyl, lower
 phenylheterocyclyl, carboxy, lower alkylsulfinyl, cyano,
 lower alkoxy carbonyl, aminocarbonyl, lower
 alkylcarbonylamino, lower haloalkyl, hydroxy, lower
 alkoxy, amino, lower cycloalkylamino, lower alkylamino,
 255 lower alkenylamino, lower alkynylamino, lower aminoalkyl,
 arylamino, lower aralkylamino, nitro, halosulfonyl, lower
 alkylcarbonyl, lower alkoxy carbonylamino, lower
 alkoxyphenylalkylamino, lower alkylaminoalkylamino, lower
 hydroxyalkylamino, lower heterocyclylamino, lower
 260 heterocyclylalkylamino, lower
 phenylalkylheterocyclylamino, lower alkylaminocarbonyl,
 lower alkoxyphenylalkylamino, hydrazinyl, lower
 alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower
 alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower

265 phenylalkyl; and

R⁴ is selected from hydrido, lower cycloalkyl, lower cycloalkenyl, aryl selected from phenyl, biphenyl, and naphthyl, and 5- or 6- membered heterocyclyl; wherein the lower cycloalkyl, lower cycloalkenyl, aryl and 5-10

270 membered heterocyclyl groups of R⁴ are optionally substituted with one or more radicals independently selected from lower alkylthio, lower alkylsulfonyl, lower alkylsulfinyl, halo, lower alkyl, lower alkynyl, lower alkoxy, lower aryloxy, lower aralkoxy, lower heterocyclyl, lower haloalkyl, amino, cyano, nitro, lower alkylamino, and hydroxy; or

275 a pharmaceutically-acceptable salt or tautomer thereof.

3. A compound of Claim 2 wherein

R¹ is selected from hydrido, methyl, ethyl, propyl, isopropyl, tert-butyl, isobutyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, 5 dichloromethyl, trichloroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, ethenyl, propenyl, ethynyl, propargyl, 1-propynyl, 2-propynyl, piperidinyl, 10 piperazinyl, morpholinyl, benzyl, phenylethyl, morpholinylmethyl, morpholinylethyl, pyrrolidinylmethyl, piperazinylmethyl, piperidinylmethyl, pyridinylmethyl, thienylmethyl, methoxymethyl, ethoxymethyl, amino, methylamino, dimethylamino, phenylamino, 15 methylaminomethyl, dimethylaminomethyl, methylaminoethyl, dimethylaminoethyl, ethylaminoethyl, diethylaminoethyl, cyclopropyl, cyclopentyl, cyclohexyl, cyclohexylmethyl, hydroxymethyl, hydroxyethyl, mercaptomethyl, and methylthiomethyl; and

20 R² is selected from hydrido, chloro, fluoro, bromo, methyl, ethyl, propyl, isopropyl, tert-butyl, isobutyl, phenyl, biphenyl, fluoromethyl, difluoromethyl,

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trifluoromethyl, chloromethyl, dichloromethyl,
trichloromethyl, pentafluoroethyl, heptafluoropropyl,
25. difluorochloromethyl, dichlorofluoromethyl,
difluoroethyl, difluoropropyl, dichloroethyl,
dichloropropyl, hydroxymethyl, hydroxyethyl, pyridinyl,
isothiazolyl, isoxazolyl, thienyl, thiazolyl, oxazolyl,
pyrimidinyl, quinolyl, isoquinolinyl, imidazolyl,
30 benzimidazolyl, furyl, pyrazinyl, piperidinyl,
piperazinyl, morpholinyl, N-methylpiperazinyl,
methoxycarbonylethyl, ethoxycarbonylethyl, N-methylamino,
N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-n-
propylamino, N,N-dimethylamino, N-methyl-N-phenylamino,
35 N-phenylamino, piperadinylamino, N-benzylamino, N-
propargylamino, cyclopropyl, cyclobutyl, cyclopentyl,
cyclohexyl, cyclopropenyl, cyclobutenyl, cyclopentenyl,
cyclohexenyl, cyclohexadienyl, aminomethyl, aminoethyl,
aminoethylamino, aminopropylamino, N,N-
40 dimethylaminoethylamino, N,N-dimethylaminopropylamino,
morpholinylethylamino, morpholinylpropylamino,
carboxymethylamino, methoxyethylamino, methoxycarbonyl,
ethoxycarbonyl, propoxycarbonyl, 1,1-
dimethylethoxycarbonyl, 1,1-
45 dimethylethoxycarbonylaminoethylamino, 1,1-
dimethylethoxycarbonylaminopropylamino,
piperazinylcarbonyl, and 1,1-
dimethylethoxycarbonylpiperazinylcarbonyl; wherein the
aryl, heteroaryl, cycloalkyl and cycloalkenyl groups are
50 optionally substituted with one or more radicals
independently selected from fluoro, chloro, bromo, keto,
methyl, ethyl, isopropyl, tert-butyl, isobutyl, benzyl,
carboxy, methoxy, ethoxy, phenoxy, benzyloxy,
trifluoromethyl, fluoromethyl, difluoromethyl,
55 dimethylamino, methoxycarbonyl, ethoxycarbonyl, and 1,1-
dimethylethylcarbonyl; or
R² is -CR⁵⁴R⁵⁵ wherein R⁵⁴ is phenyl and R⁵⁵ is hydroxy;
and

R³ is selected from pyridinyl, pyrimidinyl, and
60 purinyl; wherein R³ is optionally substituted with one or
more radicals independently selected from methylthio,
methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,
aminosulfonyl, methyl, ethyl, isopropyl, tert-butyl,
isobutyl, cyano, methoxycarbonyl, ethoxycarbonyl,
65 aminocarbonyl, methylcarbonylamino, trifluoromethyl,
difluoromethyl, fluoromethyl, trichloromethyl,
dichloromethyl, chloromethyl, hydroxy,
fluorophenylmethyl, fluorophenylethyl,
chlorophenylmethyl, chlorophenylethyl,
70 fluorophenylethenyl, chlorophenylethenyl,
fluorophenylpyrazolyl, chlorophenylpyrazolyl, carboxy,
methoxy, ethoxy, propyloxy, n-butoxy, methylamino,
ethylamino, dimethylamino, diethylamino, 2-
methylbutylamino, propargylamino, aminomethyl,
75 aminoethyl, N-methyl-N-phenylamino, phenylamino,
diphenylamino, benzylamino, phenethylamino,
cyclopropylamino, nitro, chlorosulfonyl, amino,
methylcarbonyl, methoxycarbonylamino,
ethoxycarbonylamino, methoxyphenylmethylamino, N,N-
80 dimethylaminoethylamino, hydroxypropylamino,
hydroxyethylamino, imidazolylethylamino,
morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,
piperidinylamino, pyridinylmethylamino,
85 phenylmethylpiperidinylamino, phenylmethylamino,
fluorophenylmethylamino, fluorophenylethylamino,
methylaminocarbonyl, ethylaminocarbonyl, methylcarbonyl,
methoxyphenylmethylamino, hydrazinyl, 1-methyl-
hydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is methylcarbonyl or
90 amino, and R⁶³ is methyl, ethyl or phenylmethyl; and
R⁴ is selected from hydrido, cyclopropyl, cyclobutyl,
cyclopentyl, cyclohexyl, cyclopropenyl, cyclobutenyl,
cyclopentenyl, cyclohexenyl, cyclohexadienyl, phenyl,
biphenyl, morpholinyl, pyrrolidinyl, piperazinyl,
piperidinyl, pyridinyl, thienyl, isothiazolyl,

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95 isoxazolyl, thiazolyl, oxazolyl, pyrimidinyl, quinolyl,
isoquinolinyl, imidazolyl, benzimidazolyl, furyl,
pyrazinyl, dihydropyranlyl, dihydropyridinyl,
dihydrofuryl, tetrahydropyranlyl, tetrahydrofuryl,
benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein
100 the cycloalkyl, cycloalkenyl, aryl and heterocyclyl
groups of R⁴ are optionally substituted with one or more
radicals independently selected from methylthio,
methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,
methyl, ethyl, isopropyl, tert-butyl, isobutyl, ethynyl,
105 methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl,
fluoromethyl, difluoromethyl, amino, cyano, nitro,
dimethylamino, and hydroxy; or
a pharmaceutically-acceptable salt or tautomer thereof.

4. A compound of Claim 3 wherein

R¹ is hydrido, methyl, ethyl, propargyl,
hydroxyethyl, dimethylaminoethyl, diethylaminoethyl or
morpholinylethyl;

5 R² is selected from hydrido, methyl, ethyl, propyl,
phenyl, trifluoromethyl, methoxycarbonylethyl, N,N-
dimethylamino, N-phenylamino, piperidinyl, piperazinyl,
pyridinyl, N-methylpiperazinyl, and piperazinylamino;
wherein the phenyl, piperidinyl, and pyridinyl groups are
10 optionally substituted with one or more radicals
independently selected from fluoro, chloro, bromo,
methyl, ethyl, and trifluoromethyl;

15 R³ is selected from pyridinyl, pyrimidinyl or
quinolinyl; wherein R³ is optionally substituted with one
or more radicals independently selected from fluoro,
bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl,
benzyl, phenethyl, acetyl, hydroxyl, methoxy,
dimethylamino, benzylamino, phenethylamino, aminomethyl,
amino, hydroxy, and methylcarbonyl;

20 R⁴ is selected from phenyl, quinolyl, biphenyl,
pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl,

dihydrobenzofuryl, and benzodioxolyl; wherein the cycloalkyl, cycloalkenyl, aryl and heterocyclyl groups of R⁴ are optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; or
25 a pharmaceutically-acceptable salt or tautomer thereof.

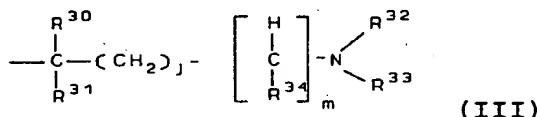
5. A compound of Claim 4 wherein
R¹ is hydrido or methyl;
R² is selected from hydrido, methyl or ethyl;
R³ is selected from pyridinyl, pyrimidinyl or
5 quinolinyl; wherein R³ is optionally substituted with one or more radicals independently selected from fluoro, bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl, benzyl, phenethyl, acetyl, hydroxyl, methoxy, dimethylamino, benzylamino, phenethylamino, aminomethyl,
10 amino, hydroxy, and methylcarbonyl;
R⁴ is selected from phenyl which is optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy,
15 trifluoromethyl, nitro, dimethylamino, and hydroxy; or a pharmaceutically-acceptable salt or tautomer thereof.

6. A compound of Claim 2 wherein
R¹ is selected from hydrido, methyl, ethyl, propyl, isopropyl, tert-butyl, isobutyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl,
5 dichloromethyl, trichloroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, ethenyl, propenyl, ethynyl, propargyl, 1-propynyl, 2-propynyl, piperidinyl,
10 piperazinyl, morpholinyl, benzyl, phenylethyl,

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- morpholinylmethyl, morpholinylethyl, pyrrolidinylmethyl,
 piperazinylmethyl, piperidinylmethyl, pyridinylmethyl,
 thienylmethyl, methoxymethyl, ethoxymethyl, amino,
 methylamino, dimethylamino, phenylamino,
 15 methylaminomethyl, dimethylaminomethyl, methylaminoethyl,
 dimethylaminoethyl, ethylaminoethyl, diethylaminoethyl,
 cyclopropyl, cyclopentyl, cyclohexyl, cyclohexylmethyl,
 hydroxymethyl, hydroxyethyl, mercaptomethyl, and
 methylthiomethyl; and

20 R² has the formula:



wherein:

j is 0, 1 or 2; and

m is 0; and

25 R³⁰ and R³¹ are independently selected from hydrogen
 and lower alkyl;

R³² is selected from hydrogen, lower alkyl, lower
 phenylalkyl, lower heterocyclylalkyl, lower
 alkoxyalkylene, aryloxyalkylene, aminoalkyl, lower

30 alkylaminoalkyl, lower phenylaminoalkyl, lower
 alkylcarbonylalkylene, lower phenylcarbonylalkylene, and
 lower heterocyclylcarbonylaminoalkylene;

R³³ is selected from hydrogen, lower alkyl, -C(O)R³⁵,
 -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰;

35 wherein R³⁵ is selected from lower alkyl, lower
 cycloalkyl, lower haloalkyl, lower alkenyl, aryl selected
 from phenyl, biphenyl and naphthyl, lower heterocyclyl,
 lower phenylalkyl, lower phenylcycloalkyl, lower
 cycloalkenylalkylene, lower heterocyclylalkylene, lower
 40 alkylphenylene, lower alkylheterocyclyl, phenylphenylene,
 lower phenylheterocyclyl, lower alkoxy, lower alenoxy,
 lower alkoxyalkylene, lower alkoxyphenylalkyl, lower

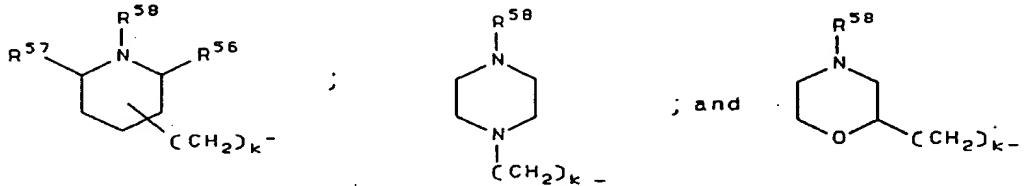
alkoxyphenylene, lower phenoxyalkylene, lower
phenylalkoxyalkylene, lower cycloalkyloxyalkylene, lower
45 alkoxycarbonyl, lower heterocyclcarbonyl, lower
alkylcarbonyloxyalkylene, lower
alkylcarbonyloxyphenylene, lower alkoxycarbonylalkylene,
lower alkoxycarbonylphenylene, lower
phenylalkoxycarbonylheterocycl, lower
50 alkylcarbonylheterocycl, lower
phenylcarbonyloxyalkylphenylene, and lower
alkylthioalkylene; wherein said aryl selected from
phenyl, biphenyl and naphthyl, lower heterocycl, lower
phenylalkyl, lower alkylphenylene, lower
55 phenylheterocycl, lower alkoxyphenylene, lower
phenoxyalkylene, lower cycloalkoxyalkylene, lower
alkoxycarbonylalkylene, and lower
alkylcarbonylheterocycl groups are optionally
substituted with one or more radicals independently
60 selected from lower alkyl, halo, lower haloalkyl, lower
alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano;
or
R³⁵ is CHR⁴⁸R⁴⁹ wherein R⁴⁸ is phenylsulfonylamino or
lower alkylphenylsulfonylamino, and R⁴⁹ is selected from
65 lower phenylalkyl, amino, lower alkylamino, and lower
phenylalkylamino; or
R³⁵ is -NR⁵⁰R⁵¹ wherein R⁵⁰ is lower alkyl, and R⁵¹ is
aryl selected from phenyl, biphenyl and naphthyl; and
wherein R³⁶ is selected from lower alkyl, lower
70 haloalkyl, aryl selected from phenyl, biphenyl and
naphthyl, lower heterocycl, lower cycloalkylalkylene,
lower alkylphenylene, lower alkenylphenylene,
phenylphenylene, lower phenylalkyl, lower phenylalkenyl,
lower heterocyclheterocycl, carboxyphenylene, lower
75 alkoxyphenylene, lower alkoxycarbonylphenylene, lower
alkylcarbonylaminophenylene, lower
alkylcarbonylaminoheterocycl, lower
phenylcarbonylaminooalkylheterocycl, lower

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alkylaminophenylene, lower alkylamino, lower
80 alkylaminophenylene, lower alkylsulfonylphenylene, lower
alkylsulfonylphenylalkyl, and lower
phenylsulfonylheterocyclyl; wherein said aryl selected
from phenyl, biphenyl and naphthyl, lower heterocyclyl,
lower cycloalkylalkylene, lower phenylalkyl, lower
85 alkylcarbonylaminothiocyclyl, and lower
alkylsulfonylphenylene groups are optionally substituted
with one or more radicals independently selected from
lower alkyl, halo, hydroxy, lower haloalkyl, lower
alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano;
90 and
wherein R³⁷ is selected from hydrogen and lower
alkyl; and
wherein R³⁸ is selected from hydrogen, lower alkyl,
lower alkenyl, aryl selected from phenyl, biphenyl and
95 naphthyl, lower heterocyclyl, lower phenylalkyl, lower
alkylphenylene, lower phenylcycloalkyl, phenylphenylene,
lower cycloalkylalkylene, lower heterocyclalkylene,
lower alkylheterocyclalkylene, lower
phenylalkylheterocyclyl, lower alkoxyalkylene, lower
100 alkoxyphenylene, lower phenoxyphenylene, phenylcarbonyl,
lower alkoxycarbonyl, lower alkoxycarbonylalkylene, lower
alkoxycarbonylphenylene, lower
alkylcarbonylcarbonylalkylene, lower alkylaminoalkylene,
lower alkylaminophenylalkyl, lower
105 alkylcarbonylaminoalkylene, lower alkylthiophenylene,
lower alkylsulfonylphenylalkyl, and lower
aminosulfonylphenylalkyl; wherein said aryl selected from
phenyl, biphenyl and naphthyl; lower heterocyclyl, lower
phenylalkyl, and lower heterocyclalkylene groups are
optionally substituted with one or more radicals
110 independently selected from lower alkyl, halo, hydroxy,
lower haloalkyl, lower alkoxy, lower haloalkoxy, keto,
amino, nitro, and cyano; or
R³⁸ is -CR⁵²R⁵³ wherein R₅₂ is lower alkoxycarbonyl,

115 and R₅₃ is lower alkylthioalkylene; or
 R³⁷ and R³⁸ together with the nitrogen atom to which
 they are attached form a 4-8 membered ring heterocycle;
 R³⁹ and R⁴⁰ have the same definition as R²⁶ and R²⁷ in
 claim 2; or

120 R² is selected from the group consisting of



(VI)

(VII)

(VIII)

wherein

125 k is an integer from 0 to 2; and
 R⁵⁶ is hydrogen or lower alkyl; and
 R⁵⁷ is hydrogen or lower alkyl; and
 R⁵⁸ is selected from hydrogen, lower alkyl, lower
 phenylalkyl, aryl selected from phenyl, biphenyl and
 naphthyl, lower heterocyclyl, lower heterocyclylalkyl,
 130 lower alkoxy carbonyl, lower alkylsulfonyl, lower
 phenylalkylsulfonyl, lower phenylsulfonyl, -C(O)R⁵⁹,
 -SO₂R⁶⁰, and -C(O)NHR⁶¹;
 wherein R⁵⁹ is selected from lower alkyl, lower
 haloalkyl, lower cycloalkyl, aryl selected from phenyl,
 135 biphenyl and naphthyl, lower heterocyclyl, lower
 alkylphenylene, lower phenylalkyl, lower
 alkylheterocyclyl, lower alkoxy, lower alkenoxy, lower
 phenylalkoxy, lower alkoxyalkylene, lower
 alkoxyphenylene, lower alkoxyphenylalkyl; wherein said
 140 aryl selected from phenyl, biphenyl and naphthyl, lower
 heterocyclyl, and lower phenylalkyl groups are optionally
 substituted with one or more radicals independently
 selected from lower alkyl, halo, hydroxy, lower

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haloalkyl, lower alkoxy, lower haloalkoxy, keto, amino,
145 nitro, and cyano; and
wherein R⁶⁰ is selected from lower alkyl, aryl
selected from phenyl, biphenyl and naphthyl, lower
heterocyclyl, lower alkylphenylene, lower
150 alkylheterocyclyl, lower phenylalkyl, lower
heterocyclylheterocyclyl, lower alkoxyphenylene, lower
alkylamino, lower alkylaminophenylene, lower
alkylsulfonylphenylene, and lower
phenylsulfonylheterocyclyl; wherein said aryl selected
155 from phenyl, biphenyl and naphthyl, lower heterocyclyl,
and lower phenylalkyl groups are optionally substituted
with one or more radicals independently selected from
lower alkyl, halo, hydroxy, lower haloalkyl, lower
alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano;
and
160 wherein R⁶¹ is selected from lower alkyl, aryl
selected from phenyl, biphenyl and napthyl, lower
alkylphenylene, and lower alkoxyphenylene; wherein said
aryl group is optionally substituted with one or more
radicals independently selected from lower alkyl, halo,
165 hydroxy, lower haloalkyl, lower alkoxy, lower haloalkoxy,
keto, amino, nitro, and cyano; and
R³ is selected from pyridinyl, pyrimidinyl, and
purinyl; wherein R³ is optionally substituted with one or
more radicals independently selected from methylthio,
170 methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,
aminosulfonyl, methyl, ethyl, isopropyl, tert-butyl,
isobutyl, cyano, methoxycarbonyl, ethoxycarbonyl,
aminocarbonyl, methylcarbonylamino, trifluoromethyl,
difluoromethyl, fluoromethyl, trichloromethyl,
175 dichloromethyl, chloromethyl, hydroxy,
fluorophenylmethyl, fluorophenylethyl,
chlorophenylmethyl, chlorophenylethyl,
fluorophenylethenyl, chlorophenylethenyl,
fluorophenylpyrazolyl, chlorophenylpyrazolyl, carboxy,

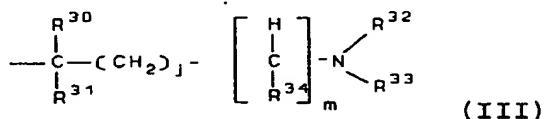
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180 methoxy, ethoxy, propyloxy, n-butoxy, methylamino,
ethylamino, dimethylamino, diethylamino, 2-
methylbutylamino, propargylamino, aminomethyl,
aminoethyl, N-methyl-N-phenylamino, phenylamino,
diphenylamino, benzylamino, phenethylamino,
185 cyclopropylamino, nitro, chlorosulfonyl, amino,
methylcarbonyl, methoxycarbonylamino,
ethoxycarbonylamino, methoxyphenylmethylethylamino, N,N-
dimethylaminoethylamino, hydroxypropylamino,
hydroxyethylamino, imidazolylethylamino,
190 morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,
piperidinylamino, pyridinylmethylethylamino,
phenylmethylpiperidinylamino, phenylmethylamino,
fluorophenylmethylethylamino, fluorophenylethylamino,
methylaminocarbonyl, ethylaminocarbonyl, methylcarbonyl,
195 methoxyphenylmethylethylamino, hydrazinyl, 1-methyl-
hydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is methylcarbonyl or
amino, and R⁶³ is methyl, ethyl or phenylmethyl; and
R⁴ is selected from hydrido, cyclopropyl, cyclobutyl,
cyclopentyl, cyclohexyl, cyclopropenyl, cyclobutenyl,
200 cyclopentenyl, cyclohexenyl, cyclohexadienyl, phenyl,
biphenyl, morpholinyl, pyrrolidinyl, piperazinyl,
piperidinyl, pyridinyl, thienyl, isothiazolyl,
isoxazolyl, thiazolyl, oxazolyl, pyrimidinyl, quinolyl,
isoquinolinyl, imidazolyl, benzimidazolyl, furyl,
205 pyrazinyl, dihydropyranyl, dihydropyridinyl,
dihydrofuryl, tetrahydropyranyl, tetrahydrofuryl,
benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein
the cycloalkyl, cycloalkenyl, aryl and heterocyclyl
groups of R⁴ are optionally substituted with one or more
210 radicals independently selected from methylthio,
methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,
methyl, ethyl, isopropyl, tert-butyl, isobutyl, ethynyl,
methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl,
fluoromethyl, difluoromethyl, amino, cyano, nitro,
215 dimethylamino, and hydroxy; or

730

a pharmaceutically-acceptable salt or tautomer thereof.

7. A compound of Claim 6 wherein
 R¹ is hydrido, methyl, ethyl, propargyl,
 hydroxyethyl, dimethylaminoethyl, diethylaminoethyl or
 morpholinylethyl;
 5 R² has the formula:



- wherein:
 j is 0, 1 or 2; and
 m is 0; and
 10 R³⁰ is hydrogen; and
 R³¹ is selected from hydrogen and lower alkyl; and
 R³² is selected from hydrogen and lower alkyl; and
 R³³ is selected from lower alkyl, -C(O)R³⁵, -C(O)OR³⁵,
 -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰;
 15 wherein R³⁵ is selected from lower alkyl, lower
 cycloalkyl, phenyl, lower heterocyclyl, lower
 alkylphenylene, lower alkoxy, lower alkenoxy, lower
 alkoxyalkylene, lower phenoxyalkylene, and lower
 phenylalkoxyalkylene; wherein said phenyl and lower
 20 phenoxyalkylene groups are optionally substituted with
 one or more radicals independently selected from lower
 alkyl, halo, and lower haloalkyl; and
 wherein R³⁶ is selected from lower alkyl, phenyl,
 lower heterocyclyl, lower alkylphenylene,
 25 phenylphenylene, lower phenylalkyl, lower
 alkylheterocyclyl, lower heterocyclheterocyclyl, lower
 alkoxyphenylene, and lower alkylamino; wherein said
 phenyl and lower heterocyclyl groups are optionally
 substituted with one or more radicals independently
 30 selected from lower alkyl, halo, hydroxy, lower

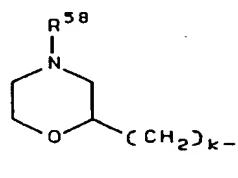
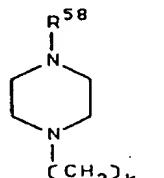
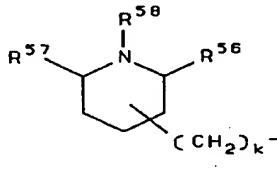
haloalkyl, lower alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano; and

wherein R³⁷ is hydrogen; and

35 wherein R³⁸ is selected from lower alkyl, phenyl, and lower alkylphenylene;

wherein R³⁹ and R⁴⁰ have the same definition as R²⁶ and R²⁷ in claim 2; or

R² is selected from the group consisting of



40 (VI)

(VII)

(VIII)

wherein

k is an integer from 0 or 1; and

R⁵⁶ is hydrogen; and

R⁵⁷ is hydrogen; and

45 R⁵⁸ is selected from -C(O)R⁵⁹ and -SO₂R⁶⁰;

wherein R⁵⁹ is selected from lower alkyl, lower cycloalkyl, phenyl, lower alkylphenylene, and lower alkoxyalkylene; wherein said phenyl group is optionally substituted with one or more radicals independently selected from lower alkyl, halo, hydroxy, lower

50 haloalkyl, lower alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano; and

wherein R⁶⁰ is selected from lower alkyl; and

55 R³ is selected from pyridinyl, pyrimidinyl or quinolinyl; wherein R³ is optionally substituted with one or more radicals independently selected from fluoro, bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl, benzyl, phenethyl, acetyl, hydroxyl, methoxy, dimethylamino, benzylamino, phenethylamino, aminomethyl,

60 amino, hydroxy, and methylcarbonyl; and
R⁴ is selected from phenyl, quinolyl, biphenyl,
pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl,
dihydrobenzofuryl, and benzodioxolyl; wherein the
cycloalkyl, cycloalkenyl, aryl and heterocyclyl groups of
65 R⁴ are optionally substituted with one or more radicals
independently selected from methylthio, fluoro, chloro,
bromo, methyl, ethyl, methoxy, ethoxy, phenoxy,
benzyloxy, trifluoromethyl, nitro, dimethylamino, and
hydroxy; or
70 a pharmaceutically-acceptable salt or tautomer
thereof.

8. A compound of Claim 7 wherein
R¹ is hydrido or methyl; and
R³ is selected from pyridinyl, pyrimidinyl or
quinolinyl; wherein R³ is optionally substituted with one
5 or more radicals independently selected from fluoro,
bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl,
benzyl, phenethyl, acetyl, hydroxyl, methoxy,
dimethylamino, benzylamino, phenethylamino, aminomethyl,
amino, hydroxy, and methylcarbonyl; and
10 R⁴ is selected from phenyl which is optionally
substituted with one or more radicals independently
selected from methylthio, fluoro, chloro, bromo, methyl,
ethyl, methoxy, ethoxy, phenoxy, benzyloxy,
trifluoromethyl, nitro, dimethylamino, and hydroxy; or
15 a pharmaceutically-acceptable salt or tautomer thereof.

9. A compound of Claim 1 wherein R¹ is hydrido.

10. A compound of Claim 2 wherein R¹ is hydrido.

11. A compound of Claim 3 wherein R¹ is hydrido.

12. A compound of Claim 6 wherein R¹ is hydrido.

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13. A compound of Claim 3 wherein R¹ is methyl or ethyl.

14. A compound of Claim 6 wherein R¹ is methyl or ethyl.

15. A compound of Claim 2 wherein R² is hydrido.

16. A compound of Claim 3 wherein R² is hydrido.

17. A compound of Claim 2 wherein R⁴ is optionally substituted phenyl.

18. A compound of Claim 3 wherein R⁴ is optionally substituted phenyl.

19. A compound of Claim 6 wherein R⁴ is optionally substituted phenyl.

20. A compound of Claim 2 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl.

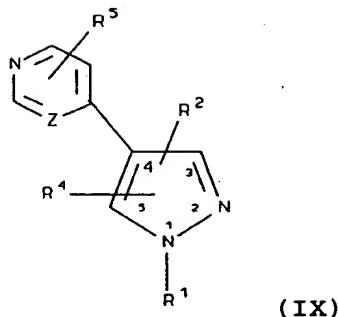
21. A compound of Claim 3 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl

22. A compound of Claim 2 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl; and R⁴ is optionally substituted phenyl.

23. A compound of Claim 3 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl; and R⁴ is optionally substituted phenyl.

24. A compound of Formula IX

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wherein

- Z represents a carbon atom or a nitrogen atom; and
- 5 R¹ is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkynyl, lower heterocycyl, lower aralkyl, lower aminoalkyl and lower alkylaminoalkyl; and
- R² is selected from hydrido, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, 5- or 6-
- 10 membered heterocycyl selected from piperidinyl, piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy carbonyl, lower alkylamino, lower alkylaminoalkyl, phenylamino, lower aralkyl, lower aralkylamino, lower
- 15 alkylaminoalkylamino, lower aminoalkyl, lower aminoalkylamino, lower alkynylamino, lower heterocyclylamino, lower heterocyclylalkyl, lower heterocyclylalkylamino, lower alkylheterocyclyl, lower carboxy cycloalkyl, lower carboxyalkylamino, lower
- 20 alkoxyalkylamino, lower alkoxy carbonylaminoalkylamino, lower heterocyclylcarbonyl, lower alkoxy carbonylheterocyclyl, and lower alkoxy carbonylheterocyclylcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or
- 25 more radicals independently selected from halo, lower

- alkyl, keto, aralkyl, carboxy, lower alkylaminoalkylamino, lower alkynylamino, lower heterocyclalkylamino, lower alkylcarbonyl and lower alkoxy carbonyl; or
- 30 R² is -CR⁵⁴R⁵⁵ wherein R⁵⁴ is phenyl and R⁵⁵ is hydroxy; and
- R⁴ is selected from hydrido, lower cycloalkyl, lower cycloalkenyl, lower cycloalkyldienyl, 5- or 6-membered heterocyclyl, and aryl selected from phenyl, biphenyl,
- 35 naphthyl; wherein R⁴ is optionally substituted at a substitutable position with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, hydroxy; and
- 40 R⁵ is selected from halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxy carbonyl, lower alkylamino, lower alkylcarbonyl, lower aralkenyl, lower
- 45 arylheterocyclyl, carboxy, lower cycloalkylamino, lower alkoxy carbonylamino, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower heterocyclalkylamino, lower aralkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower
- 50 alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower phenylalkyl; or a pharmaceutically-acceptable salt or tautomer thereof.

25. A compound of Claim 24 wherein
- R¹ is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and
- R² is selected from hydrido, methyl, ethyl, propyl,
- 5 phenyl, trifluoromethyl, hydroxyethyl, methoxycarbonylethyl, ethoxycarbonylethyl, N-methylamino,

N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N-phenylamino, aminomethyl, aminoethyl, aminoethylamino, aminopropylamino, propargylamino,
10 benzylamino, dimethylaminopropylamino, morpholinylpropylamino, morpholinylethylamino, piperidinyl, piperazinyl, imidazolyl, morpholinyl, pyridinyl, carboxymethylamino, methoxyethylamino, (1,1-dimethyl)ethylcarbonyl, (1,1-
15 dimethyl)ethylcarbonylaminopropylamino, (1,1-dimethyl)ethylcarbonylaminooethylamino, piperazinylcarbonyl, 1,1-dimethyl-ethylpiperazinylcarbonyl; wherein the phenyl, piperidinyl, piperazinyl, imidazolyl, morpholinyl, and
20 pyridinyl groups are optionally substituted with one or more radicals independently selected from fluoro, chloro, bromo, keto, methyl, ethyl, trifluoromethyl, benzyl, methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-dimethyl)ethoxycarbonyl; and
25 R⁴ is selected from cyclohexyl, cyclohexenyl, cyclohexadienyl, phenyl, quinolyl, biphenyl, pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein R⁴ is optionally substituted with one or more radicals
30 independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; and
R⁵ is selected from fluoro, chloro, bromo, methyl, 35 fluorophenylethyl, fluorophenylethenyl, fluorophenylpyrazolyl, cyano, methoxycarbonyl, aminocarbonyl, acetyl, hydroxy, carboxy, methoxy, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino,
40 hydroxyethylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino,

phenylmethylpiperidinylamino, aminomethyl,
cyclopropylamino, amino, hydroxy, methylcarbonyl,
45 ethoxycarbonylamino, methoxyphenylmethylamino,
phenylmethylamino, fluorophenylmethylamino,
fluorophenylethylamino, methylaminocarbonyl,
methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or
NR⁶²R⁶³ wherein R⁶² is methylcarbonyl or amino, and R⁶³ is
50 methyl or benzyl; or
a pharmaceutically-acceptable salt or tautomer thereof.

26. A compound of Claim 24 wherein R¹ is hydrido.

27. A compound of Claim 25 wherein R¹ is hydrido.

28. A compound of Claim 24 wherein R¹ is lower alkyl.

29. A compound of Claim 25 wherein R¹ is lower alkyl.

30. A compound of Claim 24 wherein R² is hydrido.

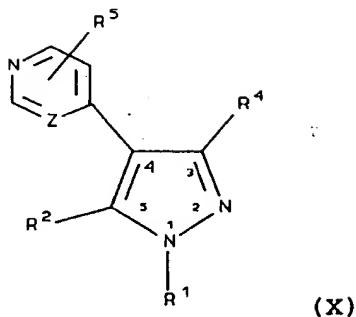
31. A compound of Claim 25 wherein R² is hydrido.

32. A compound of Claim 24 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl.

33. A compound of Claim 25 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl.

34. A compound of Claim 25 wherein Z represents a carbon atom.

35. A compound of Formula X



wherein

- Z represents a carbon atom or a nitrogen atom; and
- 5 R¹ is selected from lower alkyl, lower hydroxyalkyl, lower alkynyl, lower aminoalkyl and lower alkylaminoalkyl; and
- 10 R² is selected from hydrido, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, 5- or 6-membered heterocyclyl selected from piperidinyl, piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy carbonyl, lower alkylamino, lower alkylaminoalkyl, phenylamino, lower aralkyl, lower aralkylamino, lower
- 15 alkylaminoalkylamino, lower aminoalkyl, lower aminoalkylamino, lower alkynylamino, lower heterocyclylamino, lower heterocyclalkyl, lower heterocyclalkylamino, lower alkylheterocyclyl, lower carboxycycloalkyl, lower carboxyalkylamino, lower
- 20 alkoxyalkylamino, lower alkoxy carbonylaminoalkylamino, lower heterocyclcarbonyl, lower alkoxy carbonylheterocyclcarbonyl, and lower alkoxy carbonylheterocyclcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or
- 25 more radicals independently selected from halo, lower

alkyl, keto, aralkyl, carboxy, lower alkylaminoalkylamino, lower alkynylamino, lower heterocyclalkylamino, lower alkylcarbonyl and lower alkoxy carbonyl; or

30 R² is -CR⁵⁴R⁵⁵ wherein R⁵⁴ is phenyl and R⁵⁵ is hydroxy; and

R⁴ is selected from 5- or 6-membered heteroaryl, and aryl selected from phenyl, biphenyl, and naphthyl; wherein R⁴ is optionally substituted with one or more

35 radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, hydroxy; and

R⁵ is selected from halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxy carbonyl, lower alkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocycl, carboxy, lower cycloalkylamino, lower alkoxy carbonylamino, lower alkoxyaralkylamino, lower

45 alkylaminoalkylamino, lower heterocyclamino, lower heterocyclalkylamino, lower aralkylheterocyclamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower

50 alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower phenylalkyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

36. A compound of Claim 35 wherein

55 R¹ is selected from methyl, ethyl, hydroxyethyl and propargyl; and

R² is selected from methyl, ethyl, propyl, phenyl, trifluoromethyl, hydroxyethyl, methoxycarbonyl ethyl, ethoxycarbonyl ethyl, N-methylamino, N,N-dimethylamino, N-

60 ethylamino, N,N-diethylamino, N-propylamino, N-phenylamino, aminomethyl, aminoethyl, aminoethylamino,

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aminopropylamino, propargylamino, benzylamino,
piperadinylamino, dimethylaminoethylamino,
dimethylaminopropylamino, morpholinylpropylamino,
65 morpholinylethylamino, piperidinyl, piperazinyl,
imidazolyl, morpholinyl, pyridinyl, N-methylpiperazinyl,
carboxymethylamino, methoxyethylamino, (1,1-
dimethyl)ethylcarbonyl, (1,1-
dimethyl)ethylcarbonylaminopropylamino, (1,1-
70 dimethyl)ethylcarbonylaminooethylamino,
piperazinylcarbonyl, and 1,1-dimethyl-
ethylpiperazinylcarbonyl; wherein the phenyl,
piperidinyl, piperazinyl, imidazolyl, morpholinyl, and
pyridinyl groups are optionally substituted with one or
75 more radicals independently selected from fluoro, chloro,
bromo, keto, methyl, ethyl, trifluoromethyl, benzyl,
methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-
dimethyl)ethoxycarbonyl; and
R⁴ is selected from phenyl, quinolyl, biphenyl,
80 pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl,
dihydrobenzofuryl, and benzodioxolyl; wherein R⁴ is
optionally substituted with one or more radicals
independently selected from methylthio, fluoro, chloro,
bromo, methyl, ethyl, methoxy, ethoxy, phenoxy,
85 benzyloxy, trifluoromethyl, nitro, dimethylamino, and
hydroxy; and
R⁵ is selected from fluoro, chloro, bromo, methyl,
fluorophenylethyl, fluorophenylethenyl,
fluorophenylpyrazolyl, cyano, methoxycarbonyl,
90 aminocarbonyl, acetyl, hydroxy, carboxy, methoxy,
methylamino, dimethylamino, 2-methylbutylamino,
ethylamino, dimethylaminoethylamino, hydroxypropylamino,
hydroxyethylamino, propargylamino, imidazolylamino,
morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,
95 piperidinylamino, pyridinylmethylamino,
phenylmethylpiperidinylamino, aminomethyl,
cyclopropylamino, amino; hydroxy, methylcarbonyl,

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ethoxycarbonylamino, methoxyphenylmethy lamino,
 phenylmethy lamino, fluorophenylmethy lamino,
 100 fluorophenylethylamino, methylaminocarbonyl,
 methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -
 $\text{NR}^{62}\text{R}^{63}$ wherein R^{62} is methylcarbonyl or amino, and R^{63} is
 methyl or benzyl; or
 a pharmaceutically-acceptable salt or tautomer thereof.

37. A compound of Claim 35 wherein R^1 is lower alkyl.

38. A compound of Claim 36 wherein R^1 is lower alkyl.

39. A compound of Claim 35 wherein R^2 is hydrido.

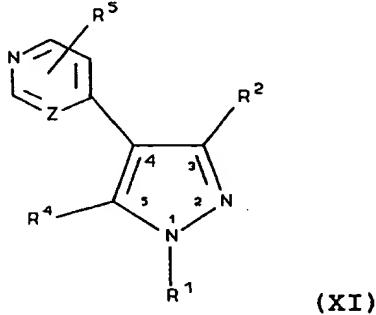
40. A compound of Claim 36 wherein R^2 is hydrido.

41. A compound of Claim 35 wherein R^1 is methyl or ethyl, and R^2 is selected from hydrido, methyl and ethyl.

42. A compound of Claim 36 wherein R^1 is methyl or ethyl, and R^2 is selected from hydrido, methyl and ethyl.

43. A compound of Claim 35 wherein Z represents a carbon atom.

44. A compound of Formula XI



wherein

Z represents a carbon atom or a nitrogen atom; and

5 R¹ is selected from lower alkyl, lower hydroxyalkyl, lower alkynyl, lower aminoalkyl and lower alkylaminoalkyl; and

R² is selected from hydrido, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, 5- or 6-membered heterocyclyl selected from piperidinyl, 10 piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy carbonyl, lower alkylamino, lower alkylaminoalkyl, phenylamino, lower aralkyl, lower aralkylamino, lower alkylaminoalkylamino, lower aminoalkylamino, lower alkynylamino, lower heterocyclylamino, lower heterocyclylalkyl, lower heterocyclylalkylamino, lower alkylheterocyclyl, lower carboxycycloalkyl, lower carboxyalkylamino, lower 20 alkoxyalkylamino, lower alkoxy carbonylaminoalkylamino, lower heterocyclylcarbonyl, lower alkoxy carbonylheterocyclyl, and lower alkoxy carbonylheterocyclylcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or 25 more radicals independently selected from halo, lower alkyl, keto, aralkyl, carboxy, lower alkylaminoalkylamino, lower alkynylamino, lower heterocyclylalkylamino, lower alkylcarbonyl and lower alkoxy carbonyl; or

30 R² is -CR⁵⁴R⁵⁵ wherein R⁵⁴ is phenyl and R⁵⁵ is hydroxy; and

R⁴ is selected from 5- or 6-membered heteroaryl, and aryl selected from phenyl, biphenyl, and naphthyl; wherein R⁴ is optionally substituted with one or more 35 radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, hydroxy; and R⁵ is selected from halo, amino, cyano,

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aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower
40 aminoalkyl, lower aralkyl, lower aralkyloxy, lower
aralkylamino, lower alkoxy carbonyl, lower alkylamino,
lower alkylcarbonyl, lower aralkenyl, lower
aryl heterocyclyl, carboxy, lower cycloalkylamino, lower
lower alkoxy carbonylamino, lower alkoxy aralkylamino, lower
45 alkylamino alkylamino, lower heterocyclylamino, lower
heterocyclylalkylamino, lower aralkyl heterocyclylamino,
lower alkylaminocarbonyl, lower alkylcarbonyl, lower
alkoxy aralkylamino, hydrazinyl, and lower
alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower
50 alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower
phenylalkyl; or
a pharmaceutically-acceptable salt or tautomer thereof.

45. A compound of Claim 44 wherein
R¹ is selected from methyl, ethyl, hydroxyethyl and
propargyl; and
R² is selected from methyl, ethyl, propyl, phenyl,
5 trifluoromethyl, hydroxyethyl, methoxycarbonylethyl,
ethoxycarbonylethyl, N-methylamino, N,N-dimethylamino, N-
ethylamino, N,N-diethylamino, N-propylamino, N-
phenylamino, aminomethyl, aminoethyl, aminoethylamino,
aminopropylamino, propargylamino, benzylamino,
10 dimethylaminopropylamino, morpholinylpropylamino,
morpholinylethylamino, piperidinyl, piperazinyl,
imidazolyl, morpholinyl, pyridinyl, carboxymethylamino,
methoxyethylamino, (1,1-dimethyl)ethylcarbonyl, (1,1-
15 dimethyl)ethylcarbonylamino propylamino, (1,1-
dimethyl)ethylcarbonylaminoethylamino,
piperazinylcarbonyl, 1,1-dimethyl-
ethylpiperazinylcarbonyl; wherein the phenyl,
piperidinyl, piperazinyl, imidazolyl, morpholinyl, and
20 pyridinyl groups are optionally substituted with one or
more radicals independently selected from fluoro, chloro,
bromo, keto, methyl, ethyl, trifluoromethyl, benzyl,

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methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-dimethyl)ethoxycarbonyl;

R⁴ is selected from phenyl, quinolyl, biphenyl, 25 pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein R⁴ is optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, 30 benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; and

R⁵ is selected from fluoro, chloro, bromo, methyl, fluorophenylethyl, fluorophenylethenyl, fluorophenylpyrazolyl, cyano, methoxycarbonyl, 35 aminocarbonyl, acetyl, hydroxy, carboxy, methoxy, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino, hydroxyethylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, 40 piperidinylamino, pyridinylmethylamino, phenylmethylpiperidinylamino, aminomethyl, cyclopropylamino, amino, hydroxy, methylcarbonyl, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, 45 fluorophenylethylamino, methylaminocarbonyl, methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is methylcarbonyl or amino, and R⁶³ is methyl or benzyl; or a pharmaceutically-acceptable salt or tautomer thereof.

46. A compound of Claim 44 wherein R¹ is lower alkyl.

47. A compound of Claim 45 wherein R¹ is lower alkyl.

48. A compound of Claim 44 wherein R² is hydrido.

49. A compound of Claim 45 wherein R² is hydrido.

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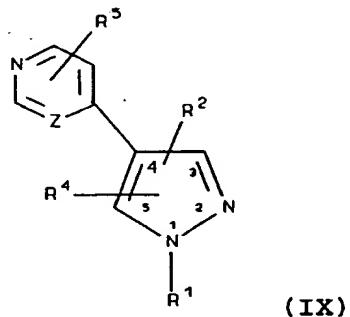
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50. A compound of Claim 44 wherein R¹ is methyl or ethyl, and R² is selected from hydrido, methyl and ethyl.

51. A compound of Claim 45 wherein R¹ is methyl or ethyl, and R² is selected from hydrido, methyl and ethyl.

52. A compound of Claim 44 wherein Z represents a carbon atom.

53. A compound of Formula IX



wherein

Z represents a carbon atom or a nitrogen atom; and
5 R¹ is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkynyl, lower aminoalkyl and lower alkylaminoalkyl; and

10 R² is selected from hydrido, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, 5- or 6-membered heterocyclyl selected from piperidinyl, piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy carbonyl, lower alkylamino, lower alkylaminoalkyl, phenylamino, lower aralkyl, lower aralkylamino, lower 15 alkylaminoalkylamino, lower aminoalkyl, lower

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- aminoalkylamino, lower alkynylamino, lower heterocycllamino, lower heterocyclalkyl, lower heterocyclalkylamino, lower alkylheterocycl, lower carboxycycloalkyl, lower carboxyalkylamino, lower alkoxyalkylamino, lower alkoxy carbonyl amine alkylamino, lower heterocyclcarbonyl, lower alkoxy carbonyl heterocyclcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or more radicals independently selected from halo, lower alkyl, keto, aralkyl, carboxy, lower alkylaminoalkylamino, lower alkynylamino, lower heterocyclalkylamino, lower alkylcarbonyl and lower alkoxy carbonyl; or
- 30 R² is -CR⁵⁴R⁵⁵ wherein R⁵⁴ is phenyl and R⁵⁵ is hydroxy; and
- R⁴ is phenyl that is optionally substituted with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, hydroxy; and
- 35 R⁵ is selected from halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxy carbonyl, lower alkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocycl, carboxy, lower cycloalkylamino, lower alkoxy carbonyl amine, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclamino, lower heterocyclalkylamino, lower aralkylheterocyclamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower phenylalkyl; or
- 40 50 a pharmaceutically-acceptable salt or tautomer

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thereof.

54. A compound of Claim 53 wherein
R¹ is selected from hydrido, methyl, ethyl,
hydroxyethyl and propargyl;
R² is selected from methyl, ethyl, propyl, phenyl,
5 trifluoromethyl, hydroxyethyl, methoxycarbonylethyl,
ethoxycarbonylethyl, N-methylamino, N,N-dimethylamino, N-
ethylamino, N,N-diethylamino, N-propylamino, N-
phenylamino, aminomethyl, aminoethyl, aminoethylamino,
aminopropylamino, propargylamino, benzylamino,
10 dimethylaminopropylamino, morpholinylpropylamino,
morpholinylethylamino, piperidinyl, piperazinyl,
imidazolyl, morpholinyl, pyridinyl, carboxymethylamino,
methoxyethylamino, (1,1-dimethyl)ethylcarbonyl, (1,1-
dimethyl)ethylcarbonylaminopropylamino, (1,1-
15 dimethyl)ethylcarbonylaminoethylamino,
piperazinylcarbonyl, 1,1-dimethyl-
ethylpiperazinylcarbonyl; wherein the phenyl,
piperidinyl, piperazinyl, imidazolyl, morpholinyl, and
pyridinyl groups are optionally substituted with one or
20 more radicals independently selected from fluoro, chloro,
bromo, keto, methyl, ethyl, trifluoromethyl, benzyl,
methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-
dimethyl)ethoxycarbonyl;
R⁴ is phenyl that is optionally substituted with one
25 or more radicals independently selected from methylthio,
fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy,
phenoxy, benzyloxy, trifluoromethyl, nitro,
dimethylamino, and hydroxy; and
R⁵ is selected from fluoro, chloro, bromo, methyl,
30 fluorophenylethyl, fluorophenylethenyl,
fluorophenylpyrazolyl, cyano, methoxycarbonyl,
aminocarbonyl, acetyl, hydroxy, carboxy, methoxy,
methylamino, dimethylamino, 2-methylbutylamino,
ethylamino, dimethylaminoethylamino, hydroxypropylamino,

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35 hydroxyethylamino, imidazolylamino,
morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,
piperidinylamino, pyridinylmethylamino,
phenylmethylpiperidinylamino; aminomethyl,
cyclopropylamino, amino, hydroxy, methylcarbonyl,
40 ethoxycarbonylamino, methoxyphenylmethylamino,
phenylmethylamino, fluorophenylmethylamino,
fluorophenylethylamino, methylaminocarbonyl,
methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -
NR⁶²R⁶³ wherein R⁶² is methylcarbonyl or amino, and R⁶³ is
45 methyl or benzyl; or
a pharmaceutically-acceptable salt or tautomer
thereof.

55. A compound of Claim 53 wherein R¹ is hydrido or lower alkyl.

56. A compound of Claim 54 wherein R¹ is hydrido or lower alkyl.

57. A compound of Claim 53 wherein R¹ is hydrido.

58. A compound of Claim 54 wherein R¹ is hydrido.

59. A compound of Claim 53 wherein R² is hydrido.

60. A compound of Claim 54 wherein R² is hydrido.

61. A compound of Claim 53 wherein R⁴ is phenyl substituted with one or more fluoro, chloro or bromo.

62. A compound of Claim 54 wherein R⁴ is phenyl substituted with one or more fluoro, chloro or bromo.

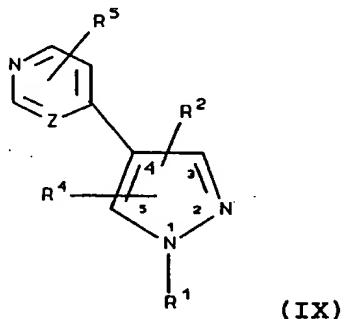
63. A compound of Claim 53 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl.

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64. A compound of Claim 54 wherein R¹ and R² are selected independently from hydrido, methyl and ethyl.

65. A compound of Claim 53 wherein Z represents a carbon atom.

66. A compound of Formula IX



wherein

Z represents a carbon atom or a nitrogen atom; and

5 R¹ is selected from hydrido, lower alkyl, lower hydroxyalkyl and lower alkynyl; and

R² is selected from hydrido and lower alkyl; and

10 R⁴ is selected from phenyl and benzodioxolyl; wherein phenyl is optionally substituted with one or more halo radicals; and

R⁵ is selected from hydrido, halo and

alkylhydrazinyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

67. A compound of Claim 66 wherein

Z represents a carbon atom; and

R¹ is selected from hydrido, methyl, hydroxyethyl, propargyl; and

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- 5 R² is hydrido; and
R⁴ is selected from phenyl and benzodioxolyl; wherein
phenyl is optionally substituted with one or more
radicals independently selected from chloro, fluoro and
bromo; and
10 R⁵ is selected from hydrido, fluoro, and 1-
methylhydrazinyl; or
a pharmaceutically-acceptable salt or tautomer
thereof.

68. A compound of Claim 67 wherein
Z represents a carbon atom; and
R¹ is selected from hydrido and methyl; and
R² is hydrido; and
5 R⁴ is selected from phenyl that is optionally
substituted with one or more radicals independently
selected from chloro, fluoro and bromo; and
R⁵ is selected from hydrido and fluoro; or
a pharmaceutically-acceptable salt or tautomer thereof.

69. A compound of Claim 1 selected from compounds,
their tautomers and their pharmaceutically acceptable
salts, of the group consisting of
4- [5- (3-fluoro-4-methoxyphenyl) -3-methyl-1H-pyrazol-4-
5 yl]pyridine;
4- (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;
4- [5-methyl-3- (2-methylphenyl) -1H-pyrazol-4-yl]pyridine;
4- [3- (4-fluorophenyl) -5-methyl-1H-pyrazol-4-yl]pyridine;
4- [5-methyl-3- (4-methylphenyl) -1H-pyrazol-4-yl]pyridine;
10 4- [5-methyl-3- [4- (methylthio)phenyl] -1H-pyrazol-4-
yl]pyridine;
4- [3- (4-chlorophenyl) -5-methyl-1H-pyrazol-4-yl]pyridine;
4- [3-methyl-5- (3-methylphenyl) -1H-pyrazol-4-yl]pyridine;
4- [5- (2,5-dimethylphenyl) -3-methyl-1H-pyrazol-4-
15 yl]pyridine;
4- [5- (1,3-benzodioxol-5-yl) -3-methyl-1H-pyrazol-4-

yl]pyridine;
4-[3-methyl-5-(4-phenoxyphenyl)-1H-pyrazol-4-yl]pyridine;
4-[5-[(1,1'-biphenyl)-4-yl]-3-methyl-1H-pyrazol-4-
20 yl]pyridine;
4-[3-methyl-5-[3-(phenoxyphenyl)-1H-pyrazol-4-
yl]pyridine;
4-[3-methyl-5-[3-(phenylmethoxy)phenyl]-1H-pyrazol-4-
yl]pyridine;
25 4-[3-methyl-5-[2-(phenylmethoxy)phenyl]-1H-pyrazol-4-
yl]pyridine;
2-[3-methyl-4-(4-pyridinyl)-1H-pyrazol-4-yl]phenol;
3-[3-methyl-4-(4-pyridinyl)-1H-pyrazol-4-yl]phenol;
1-hydroxy-4-(3-methyl-5-phenyl-1H-pyrazol-4-
30 yl)pyridinium;
5-(4-fluorophenyl)-N, N-dimethyl-4-(4-pyridinyl)-1H-
pyrazol-3-amine;
5-(4-fluorophenyl)-N-phenyl-4-(4-pyridinyl)-1H-pyrazol-3-
amine; 4-[5-(4-fluorophenyl)-3-phenyl-1H-pyrazol-4-
35 yl]pyridine;
4-[5-(3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-4-
yl]pyridine; 4-[3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-
pyrazol-5-yl]pyridine;
4-(5-cyclohexyl)-3-methyl-1H-pyrazol-4-yl)pyridine;
40 4-[5-(3-fluoro-5-methoxyphenyl)-3-methyl-1H-pyrazol-4-
yl]pyridine;
4-[5-(3-methylphenyl)-3-propyl-1H-pyrazol-4-yl]pyridine;
4-[(3-methyl-5-phenyl-1H-pyrazol-4-yl)methyl]pyridine;
4-[3,5-bis(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;
45 4-[4-methyl-2-(2-trifluorophenyl)-1H-pyrazol-4-
yl]pyridine;
4-[3-(2-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;
4-[5-methyl-3-(2,4-dimethylphenyl)-1H-pyrazol-4-
yl]pyridine;
50 4-[5-(4-chlorophenyl)-1,3-dimethyl-1H-pyrazol-4-
yl]pyridine;
4-[3-(3-fluoro-2-methylphenyl)-5-methyl-1H-pyrazol-4-

yl]pyridine;
4-[3-(3,5-dimethylphenyl)-5-methyl-1H-pyrazol-4-
55 yl]pyridine;
4-[3-(3,5-dimethoxyphenyl)-5-methyl-1H-pyrazol-4-
yl]pyridine;
4-[5-methyl-3-(3-nitrophenyl)-1H-pyrazol-4-yl]pyridine;
N,N-dimethyl-4-[5-methyl-4-(4-pyridinyl)-1H-pyrazol-3
60 60 yl]benzenamine;
4-[3-(2,3-dihydrobenzofuran-5-yl)-5-methyl-1H-pyrazol-4-
yl]pyridine;
4-[3-(4-bromophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-(2-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;
65 65 4-[3-(3-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-methyl-5-[3-(trifluoromethyl)phenyl]-1H-pyrazol-4-
yl]pyridine;
4-(3-ethyl-4-phenyl-1H-pyrazol-4-yl)pyridine;
4-[5-(3-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;
70 70 4-[3-ethyl-5-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;
4-[5-(3,4-difluorophenyl)-3-methyl-1H-pyrazol-4-
yl]pyridine;
4-[5-(3-ethoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-methyl-5-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-
75 75 yl]pyridine;
4-[3-methyl-5-(3-thienyl)-1H-pyrazol-4-yl]pyridine;
4-[5-(2,4-dichlorophenyl)-3-methyl-1H-pyrazol-4-
yl]pyridine;
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;
80 80 4-[5-(3-chloro-4-methoxyphenyl)-3-methyl-1H-pyrazol-4-
yl]pyridine;
ethyl 3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazole-5-
propanoate;
4-[3-(4-fluorophenyl)-1-methyl-pyrazol-4-yl]pyridine;
85 85 5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-
2-amine;
5-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-yl]pyrimidin-
2-amine;

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5-[3-methyl-5-(2-methylphenyl)-1H-pyrazol-4-yl]pyrimidin-
90 2-amine;
5-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-
2-amine;
5-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-
2-amine;
95 5-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-
2-amine;
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
amine;
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
100 amine;
4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
amine;
4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
amine;
105 4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
amine;
4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
amine;
4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-
110 2-amine;
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-
methoxypyridine;
2-methoxy-5-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-
yl]pyridine;
115 2-methoxy-5-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-
yl]pyridine;
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-
methoxypyridine;
2-methoxy-4-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-
120 yl]pyridine;
2-methoxy-4-[3-methyl-5-(2-methylphenyl)-1H-pyrazol-4-
yl]pyridine;
4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-
methoxypyridine;

754

- 125 4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-methoxypyridine;
 2-methoxy-4-[3-methyl-5-(4-methylphenyl)-1H-pyrazol-4-yl]pyridine;
 5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
130 4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
 4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
135 4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
 4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
 4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
140 4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;
 5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
145 4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
 4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
 4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
150 4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
 4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
155 4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;
 5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;
 4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;
160

- 4- [5- (3-methylphenyl) -3-methyl-1H-pyrazol-4-yl] pyridine-
2-carboxamide;
4- [5- (2-methylphenyl) -3-methyl-1H-pyrazol-4-yl] pyridine-
2-carboxamide;
165 4- [5- (4-chlorophenyl) -3-methyl-1H-pyrazol-4-yl] pyridine-
2-carboxamide;
4- [5- (4-fluorophenyl) -3-methyl-1H-pyrazol-4-yl] pyridine-
2-carboxamide;
4- [5- (4-methoxyphenyl) -3-methyl-1H-pyrazol-4-yl] pyridine-
170 2-carboxamide;
4- [5- (3-fluoro-4-methoxyphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (4-fluoro-3-methoxyphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
175 4- [5- (4-chloro-3-methoxyphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (2,3-dihydrobenzofuran-6-yl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (benzofuran-6-yl) -3-methyl-1H-pyrazol-4-yl] pyridine;
180 4- [5- (3-fluoro-5-methoxyphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (3-chloro-5-methoxyphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (1-cyclohexen-1-yl) -3-methyl-1H-pyrazol-4-
185 yl] pyridine;
4- [5- (1,3-cyclohexadien-1-yl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (5,6-dihydro-2H-pyran-4-yl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
190 4- (5-cyclohexyl-3-methyl-1H-pyrazol-4-yl) pyridine;
4- [5- (4-methoxy-3-methylphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (3-methoxy-4-methylphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;
195 4- [5- (3-methoxy-5-methylphenyl) -3-methyl-1H-pyrazol-4-
yl] pyridine;

4 - [5 - (3-furyl) - 3-methyl-1H-pyrazol-4-yl]pyridine;
2-methyl-4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;
2-methoxy-4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;
200 methyl 4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-2-carboxylate;
4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-2-carboxamide;
1 - [4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridin-2-
205 yl]ethanone;
N,N-dimethyl-4 - (3-methyl-5-phenyl-1H-pyrazol-2-
yl)pyridin-2-amine;
3-methyl-4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;
3-methoxy-4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;
210 methyl 4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-3-carboxylate;
4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-3-carboxamide;
1 - [4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridin-3-
215 yl]ethanone;
3-bromo-4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;
N,N-dimethyl-4 - (3-methyl-5-phenyl-1H-pyrazol-2-
yl)pyridin-3-amine;
2-methyl-4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidine;
220 4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidine;
2-methoxy-4 - (3-methyl-5-phenyl-1H-pyrazol-4-
yl)pyrimidine;
4 - (3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine;
N,N-dimethyl-4 - (3-methyl-5-phenyl-1H-pyrazol-4-
225 yl)pyrimidin-2-amine;
4 - (5,6-dihydro-2H-pyran-4-yl)-3-methyl-5-phenyl-1H-pyrazole;
3-methyl-5-phenyl-4 - (3-thienyl)-1H-pyrazole;
4 - (3-furyl)-3-methyl-5-phenyl-1H-pyrazole;
230 3-methyl-5-phenyl-4 - (2-thienyl)-1H-pyrazole;
4 - (2-furyl)-3-methyl-5-phenyl-1H-pyrazole;
4 - (3-isothiazolyl)-3-methyl-5-phenyl-1H-pyrazole

4-(3-isoxazolyl)-3-methyl-5-phenyl-1H-pyrazole;
4-(5-isothiazolyl)-3-methyl-5-phenyl-1H-pyrazole;
235 4-(5-isoxazolyl)-3-methyl-5-phenyl-1H-pyrazole;
3-methyl-5-phenyl-4-(5-thiazolyl)-1H-pyrazole;
3-methyl-4-(5-oxazolyl)-5-phenyl-1H-pyrazole;
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;
2-methyl-4-[3-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;
240 4-(1-methyl-3-phenyl-1H-pyrazol-4-yl)pyridine;
4-(3-phenyl-1H-pyrazol-4-yl)pyridine;
2-methyl-4-(3-phenyl-1H-pyrazol-4-yl)pyridine;
4-[3-(3-chlorophenyl)-1-methyl-pyrazol-4-yl]pyridine;
4-[3-(4-chlorophenyl)-1-methyl-pyrazol-4-yl]pyridine;
245 4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-2-methylpyridine;
4-[3-(3-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-(3-fluorophenyl)-1H-pyrazol-4-yl]pyridine;
250 4-[3-(3-chlorophenyl)-1-methyl-pyrazol-4-yl]-2-
methylpyridine;
5-(4-chlorophenyl)-N-phenyl-4-(4-pyridinyl)-1H-pyrazol-3-
amine;
5-(4-chlorophenyl)-N-methyl-4-(4-pyridinyl)-1H-pyrazol-3-
255 amine;
5-(4-chlorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-
pyrazol-3-amine dihydrate;
5-(3-fluorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-
pyrazol-3-amine;
260 N,N-dimethyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-
pyrazol-3-amine;
N-methyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-
amine;
N-ethyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-
265 amine;
N,N-diethyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-
pyrazol-3-amine;
5-(4-chlorophenyl)-N,N-diethyl-4-(4-pyridinyl)-1H-

- pyrazol-3-amine;
270 4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-
y1]morpholine;
5-(4-chlorophenyl)-N-propyl-4-(4-pyridinyl)-1H-pyrazol-3-
amine;
5-(4-chlorophenyl)-N-(phenylmethyl)-4-(4-pyridinyl)-1H-
275 pyrazol-3-amine hydrate (2:1);
5-(4-chlorophenyl)-N-(2-methoxyethyl)-4-(4-pyridinyl)-1H-
pyrazol-3-amine monohydrate;
1,1-dimethylethyl-4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-
1H-pyrazol-3-yl]-1-piperazinecarboxylate;
280 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-
y1]piperazine trihydrochloride;
1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-
methylpiperazine;
1,1-dimethylethyl 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-
285 1H-pyrazol-3-yl]-1-piperazinecarboxylate;
1-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-
y1]piperazine trihydrochloride;
1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-
y1]piperazine;
290 N-[5-(4-chlorophenyl)-4-[2-(phenylmethyl)amino]-4-
pyridinyl]-1H-pyrazol-3-yl]-1,3-propanediamine,
trihydrochloride;
1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-
(phenylmethyl)piperazine;
295 4-[3-(4-fluorophenyl)-5-(1-piperazinyl)-1H-pyrazol-4-
y1]pyrimidine, dihydrochloride;
1,1-dimethylethyl [3-[[5-(4-chlorophenyl)-4-(4-
pyridinyl)-1H-pyrazol-3-yl]amino]propyl] carbamate;
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-
300 1,3-propanediamine, trihydrochloride monohydrate;
1,1-dimethylethyl [2-[[5-(4-chlorophenyl)-4-(4-
pyridinyl)-1H-pyrazol-3-yl]amino]ethyl] carbamate;
1,1-dimethylethyl 4-[5-(4-chlorophenyl)-1-(2-
hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-

305 piperazinecarboxylate;
1,1-dimethylethyl 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-piperazinecarboxylate;
1,1-dimethylethyl [3-[[5-(4-chlorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-pyrazol-3-yl]amino]propyl]carbamate;
310 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-ethylpiperazine;
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2-ethanediamine;
4-[3-(2,6-difluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;
315 4-[3-(3-ethylphenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-(3-chlorophenyl)-5-ethyl-1H-pyrazol-4-yl]pyridine;
4-[3-ethyl-5-(3-ethylphenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(4-chlorophenyl)-5-(1-methylethyl)-1H-pyrazol-4-
320 pyridine;
4-[3-cyclopropyl-5-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(4-fluorophenyl)-5-(trifluoromethyl)-1H-pyrazol-4-
yl]pyridine;
325 4-[5-(cyclopropyl-3-(4-(fluorophenyl)-1-methyl-1H-pyrazol-4-yl)pyridine;
5-cyclopropyl-3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol;
3-(4-fluorophenyl)-5-(2-methoxy-4-pyridinyl)-4-(4-
330 pyridinyl)-1H-pyrazole-1-ethanol;
4-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-
1H-pyrazol-5-yl]-2(1H)-pyridinone;
1-acetyl-4-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]-2(1H)-pyridinone;
335 Ethyl 2-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]cyclopropanecarboxylate;
2-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]cyclopropanecarboxylic acid;
3-(4-fluorophenyl)-5-(4-imidazolyl)-4-(4-pyridinyl)-1H-
340 pyrazole-1-ethanol;

760

- 4- [3- (4-chloro-3-methylphenyl) -1H-pyrazol-4-yl] pyridine
5- (4-fluorophenyl) -4- (4-pyridinyl) -1H-pyrazole-3-
carboxylic acid;
5- (4-fluorophenyl) -4- (4-pyridinyl) -1H-pyrazole-3-
345 methanol;
1- [(5- (4-fluorophenyl) -4- (4-pyridinyl) -1H-pyrazol-3-
yl] carbonyl] piperazine;
1,1-dimethylethyl 4- [(5- (4-fluorophenyl) -4- (4-pyridinyl) -
1H-pyrazol-3-yl] carbonyl] -1-piperazinecarboxylate;
350 4- (1,5-dimethyl-3-phenyl-1H-pyrazol-4-yl) pyridine;
4- (1,3-dimethyl-5-phenyl-1H-pyrazol-4-yl) pyridine;
4- [3- (4-chlorophenyl) -1,5-dimethyl-1H-pyrazol-4-
yl] pyridine;
4- [5- (4-chlorophenyl) -1,3-dimethyl-1H-pyrazol-4-
355 yl] pyridine;
4- [5-ethyl-1-methyl-3- (3-methylphenyl) -1H-pyrazol-4-
yl] pyridine;
4- [3-ethyl-1-methyl-5- (3-methylphenyl) -1H-pyrazol-4-
yl] pyridine;
360 4- [3- (4-chlorophenyl) -1-ethyl-5-methyl-1H-pyrazol-4-
yl] pyridine;
4- [3- (4-chlorophenyl) -2-ethyl-5-methyl-1H-pyrazol-4-
yl] pyridine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] pyridine;
365 4- [3- (2-chlorophenyl) -1H-pyrazol-4-yl] pyridine;
3- (4-fluorophenyl) -4- (4-pyridinyl) -1H-pyrazole-1-ethanol;
3- (4-fluorophenyl) -4- (4-pyrimidinyl) -1H-pyrazole-1-
ethanol;
4- [3- (4-fluorophenyl) -1-methyl-1H-pyrazol-4-yl] pyridine;
370 2- [(4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2-
pyridinyl] amino] -1-butanol;
4- [5-bromo-3- (4-fluorophenyl) -1-methyl-1H-pyrazol-4-
yl] pyridine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2-
375 pyridinecarbonitrile;
4- [2- [3- (4-fluorophenyl) -4- (4-pyridinyl) -1H-pyrazol-1-

yl]ethyl)morpholine;
3-(4-fluorophenyl)-1-methyl- α -phenyl-4-(4-pyridinyl)-1H-pyrazole-5-methanol;
380 N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-morpholineethanamine;
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-2(1H)-pyridinone
hydrazone;
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-N-(phenylmethyl)-
385 2-pyridinamine;
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-N-(phenylethyl)-2-pyridinamine;
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-N-ethyl-2-pyridinamine;
390 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinecarboxamide;
Methyl 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinecarboxylate;
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-methyl-2-
395 pyridinecarboxamide;
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinecarboxylic acid;
4-[3-(3-fluorophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(1,3-benzodioxol-5-yl)-1H-pyrazol-4-yl]pyridine;
400 4-[3-(3-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(1,3-benzodioxol-5-yl)-1-methyl-1H-pyrazol-4-yl]pyridine;
4-[3-(4-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
405 4-[3-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-methylpyridine; 4-[5-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-methylpyridine;
4-[3-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
4-[5-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
410 2-methyl-4-[1-methyl-3-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;
2-methyl-4-[1-methyl-5-(3-methylphenyl)-1H-pyrazol-4-

-yl]pyridine;
4-(3-phenyl-1H-pyrazol-4-yl)pyridine;
415 4-[3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]pyridine
;
4-[1-methyl-3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]
]pyridine;
4-[3-(3,4-difluorophenyl)-1H-pyrazol-4-yl]pyridine;
420 4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-fluoropyridine;
4-[3-(4-bromophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(3,4-difluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyri
ne;
4-[3-(4-bromophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
425 (E)-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-(2-phenyleth
enyl)pyridine;
(S)-4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-N-(2-methylbut
yl)-2-pyridinamine;
430 4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-N-[(4-methoxy-
phenyl)methyl]-2-pyridinamine;
N-[4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-
2-pyridinemethanamine;
N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-
2-pyridinemethanamine;
435 2-fluoro-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(4-iodophenyl)-1H-pyrazol-4-yl]pyridine;
4-[3-(4-iodophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;
4-[1-methyl-3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]
]pyridine;
440 N-[1-(4-fluorophenyl)ethyl]-4-[3-(4-fluorophenyl)-1H-pyra
zol-4-yl]-2-pyridinamine;
N-[(3-fluorophenyl)methyl]-4-[3-(4-fluorophenyl)-1H-pyra
zol-4-yl]-2-pyridinamine;
4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-(1-
445 methylhydrazino)pyridine;
2-fluoro-4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]p
yridine;
4-[3-(3,4-difluorophenyl)-1H-pyrazol-4-yl]-2-fluoro-

pyridine;

450 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-3-methylpyridine;
 4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-3-methyl-
 pyridine;
 4-[3-(3,4-difluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-flu-
 oropyridine;

455 3-(4-fluorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-pyra-
 zole-1-ethanamine;
 2-[2-(4-fluorophenyl)ethyl]-4-[3-(4-fluorophenyl)-1-
 methyl-1H-pyrazol-4-yl]pyridine;

460 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[1-
 (phenylmethyl)-4-piperidinyl]-2-pyridinamine;
 N'-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-
 N,N-dimethyl-1,2-ethanediamine;
 2,4-bis[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;
 N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-4-
465 morpholineethanamine;
 3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-pyrazole-
 1-ethanol;
 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[2-(1H-imidazol-
 1-yl)ethyl]-2-pyridinamine;

470 4-[2-[3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-
 pyrazol-1-yl]ethyl]morpholine;
 (E)-3-(4-fluorophenyl)-4-[2-[2-(4-fluorophenyl)ethenyl]-
 4-pyridinyl]-1H-pyrazole-1-ethanol;
 3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-N,N-dimethyl-
475 1H-pyrazole-1-ethanamine;
 3-(4-fluorophenyl)-4-[2-[2-(4-fluorophenyl)ethyl]-4-
 pyridinyl]-1H-pyrazole-1-ethanol;
 4-[1-[2-(dimethylamino)ethyl]-3-(4-fluorophenyl)-1H-
 pyrazol-4-yl]-N,N-dimethyl-2-pyridinamine;

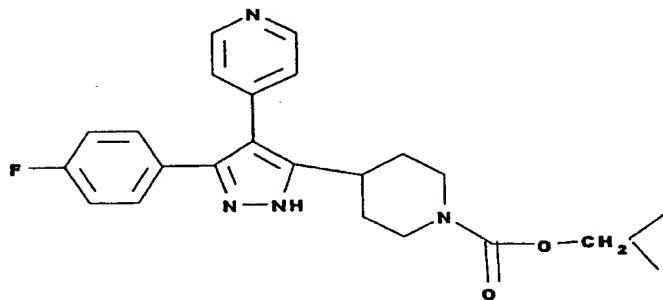
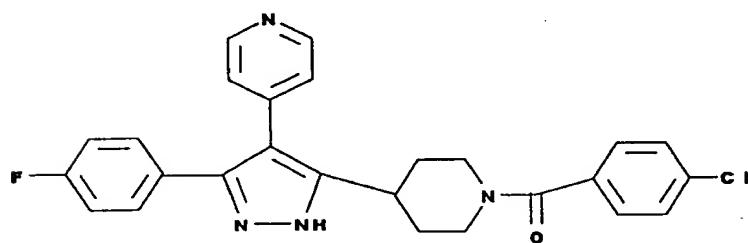
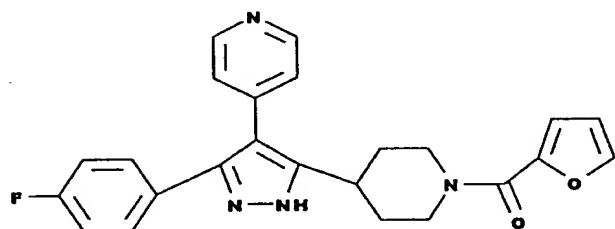
480 4-[1-[2-(dimethylamino)ethyl]-3-(4-fluorophenyl)-1H-
 pyrazol-4-yl]-N-[(4-fluorophenyl)methyl]-2-pyridinamine;
 3-(4-fluorophenyl)-4-[2-[2-(4-fluorophenyl)ethyl]-4-
 pyridinyl]-N,N-dimethyl-1H-pyrazole-1-ethanamine;
 N-[(4-fluorophenyl)methyl]-4-[3(or 5)-(4-fluorophenyl)-1-

764

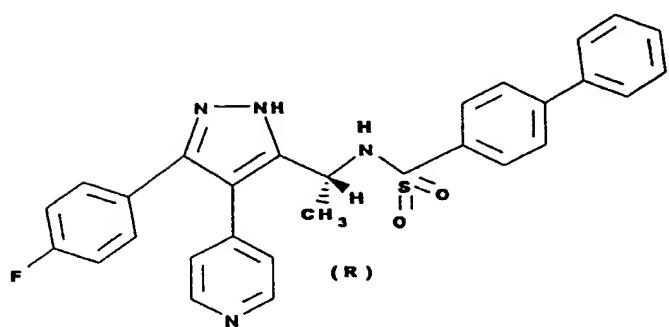
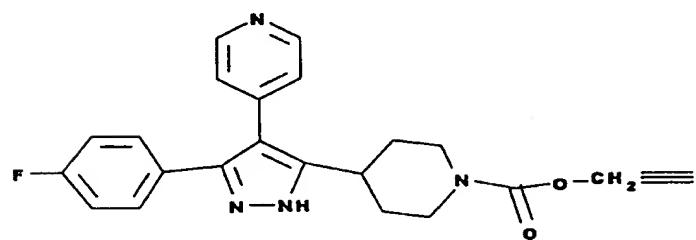
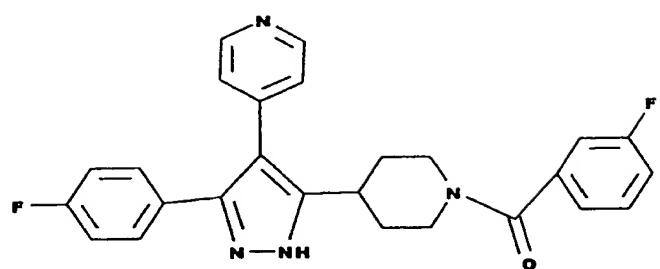
- 485 [[2-(4-morpholinyl)ethyl]-1H-pyrazol-4-yl]-2-pyridinamine;
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-4-piperadinyl-2-pyridinamine;
N,N-diethyl-3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-pyrazole-1-ethanamine;
4-[1-[2-(diethylamino)ethyl]-3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[(4-fluorophenyl)methyl]-2-pyridinamine;
2-[[4-[3-(4-(fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]amino]ethanol;
495 2-[[4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-pyridinyl]amino]ethanol;
3-[[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]amino]-1-propanol;
3-(4-fluorophenyl)-4-[2-[[4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;
500 5-(4-fluorophenyl)-4-[2-[[4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;
N,N-diethyl-3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanamine;
505 N-[(4-fluorophenyl)methyl]-4-[3-(4-fluorophenyl)-1-[2-(4-morpholinyl)ethyl]-1H-pyrazol-4-yl]-2-pyridinamine;
N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-morpholinepropanamine;
N'-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-
510 N,N-dimethyl-1,3-propanediamine;
5-(4-fluorophenyl)-N-2-propynyl-4-(4-pyridinyl)-1H-pyrazol-3-amine;
3-(4-fluorophenyl)-4-[2-[[4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;
515 5-(4-fluorophenyl)-4-[2-[[4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;
4-[3-[(4-fluorophenyl)-1H-pyrazol-4-yl]quinoline;
N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]glycine methyl ester;
520 N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-

yl] glycine;
4- [3- (4-fluorophenyl) -1- (2-propynyl) -1H-pyrazol-4-
yl] pyridine;
4- [5- (4-fluorophenyl) -1- (2-propynyl) -1H-pyrazol-4-
525 yl] pyridine;
4,4'-(1H-pyrazole-3,4-diyl)bis[pyridine];
4- [3- (3,4-dichlorophenyl) -1H-pyrazol-4-yl] pyridine;
N- [5- (4-chlorophenyl) -4- (4-pyridinyl) -1H-pyrazol-3-yl] -4-
piperidinamine;
530 2-Chloro-4- [3- (4-fluorophenyl) -1H-pyrazol-4-
yl] pyrimidine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2 (1H) -pyrimidinone
hydrazone;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -N,N-dimethyl-2-
535 pyrimidinamine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -N-methyl-2-
pyrimidinamine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -N- (phenylmethyl) -
2-pyrimidinamine;
540 N-cyclopropyl-4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2-
pyrimidinamine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -N- [(4-
methoxyphenyl)methyl] -2-pyrimidinamine;
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2-pyrimidinamine;
545 N- [4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2-pyrimidinyl] -
N- (phenylmethyl) acetamide;
Ethyl [4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] -2-
pyrimidinyl] carbamate;
4- [3- (3-methylphenyl) -1H-pyrazol-4-yl] pyrimidine;
550 4- [3- (4-chlorophenyl) -1H-pyrazol-4-yl] pyrimidine;
4- [3- (3-fluorophenyl) -1H-pyrazol-4-yl] pyrimidine; and
4- [3- (4-fluorophenyl) -1H-pyrazol-4-yl] pyrimidine.

70. A compound of Claim 1 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of

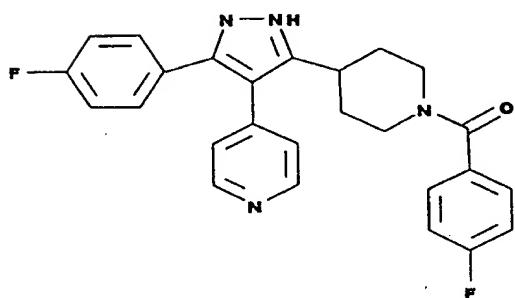
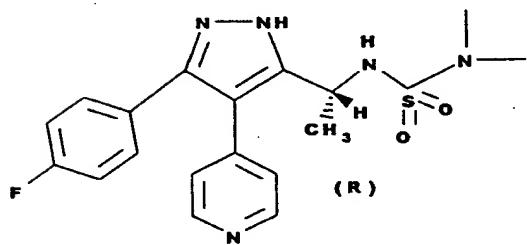
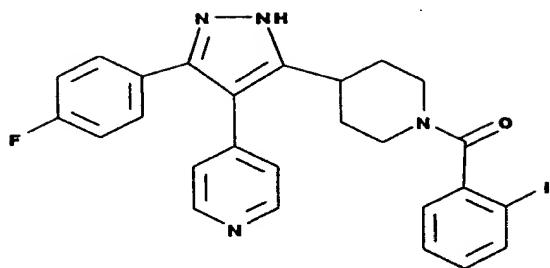


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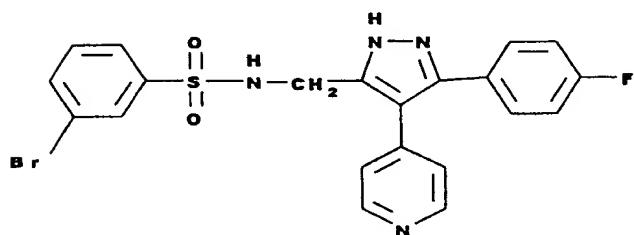
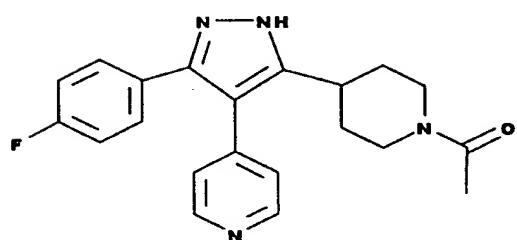
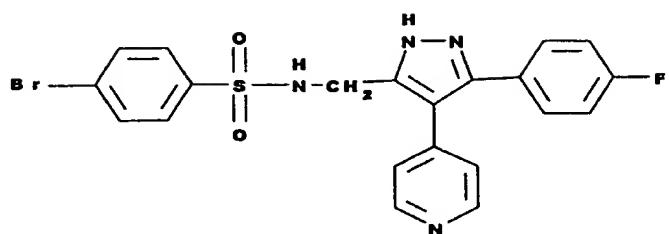
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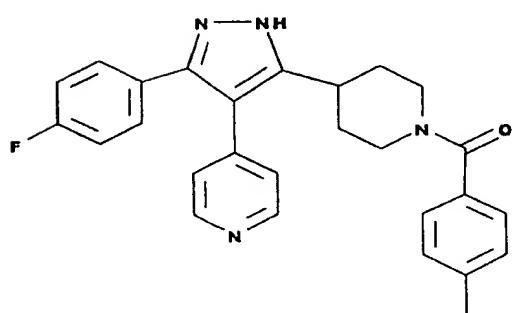
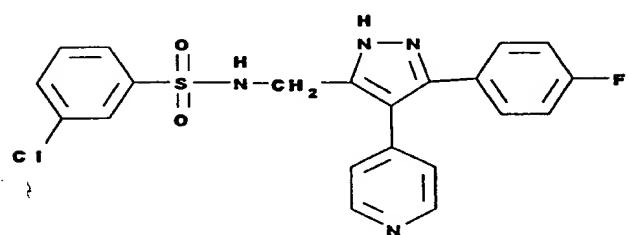
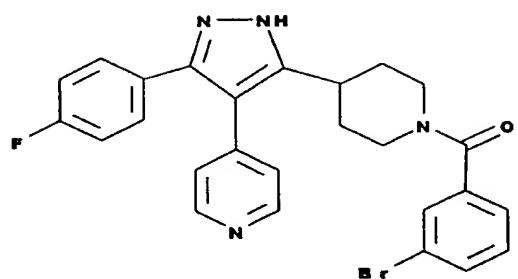


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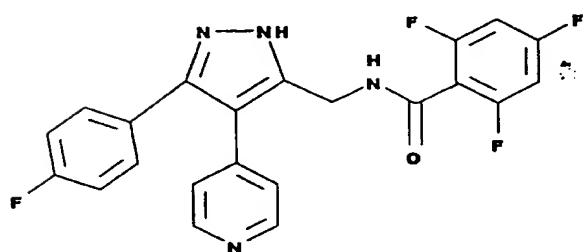
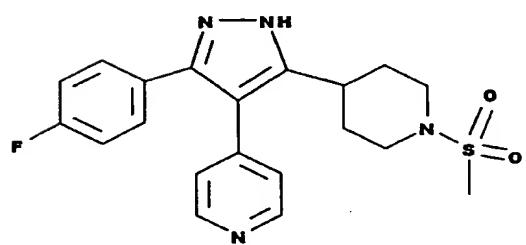
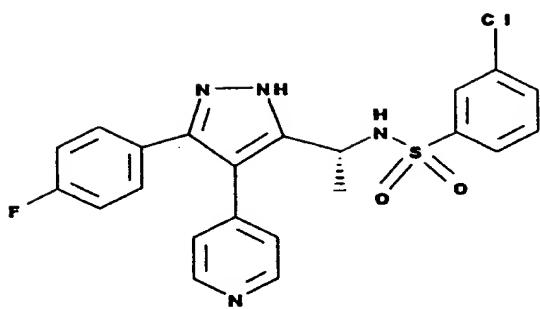
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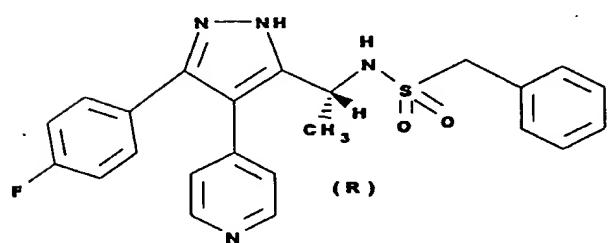
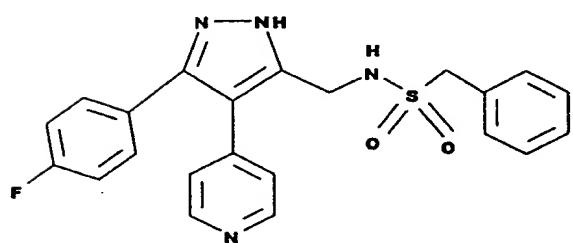
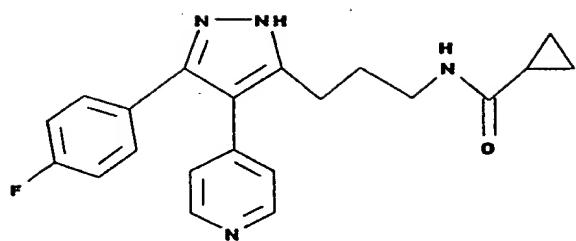


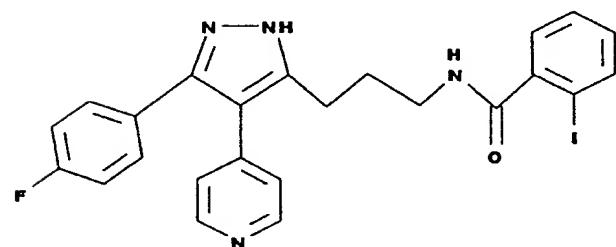
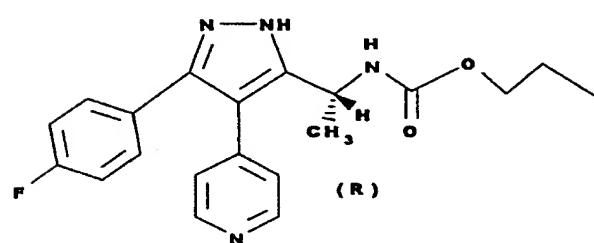
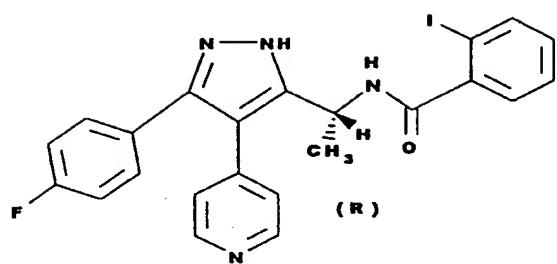
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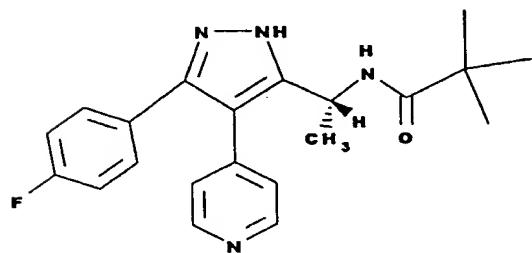
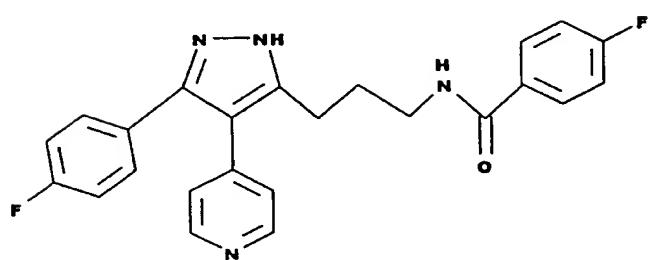
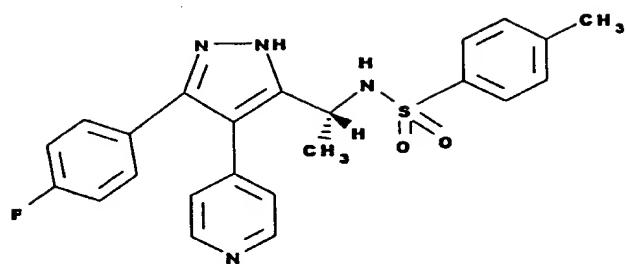


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71. A compound of claim 1 that is 4-[5-(4-fluorophenyl)-1-(2-propynyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

72. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1-(2-propynyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

73. A compound of claim 1 that is 3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol or a pharmaceutically-acceptable salt or a tautomer thereof.

74. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-(1-methylhydrazino)pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

75. A compound of claim 1 that is 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]piperazine or a pharmaceutically-acceptable salt or a tautomer thereof.

76. A compound of claim 1 that is 4-[3-cyclopropyl-5-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

77. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

78. A compound of claim 1 that is 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine or a pharmaceutically-acceptable salt or a tautomer thereof.

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79. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyrimidine or a pharmaceutically-acceptable salt or a tautomer thereof.

80. A compound of claim 1 that is 2-fluoro-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

81. A compound of claim 1 that is 4-[3-(3,4-difluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

82. A compound of claim 1 that is 4-[3-(4-bromophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

83. A compound of claim 1 that is 4-[3-(4-chlorophenyl)1H-pyrazol-4-yl]-2-fluoropyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

84. A compound of claim 1 that is 4-[3-(1,3-benzodioxol-5-yl)-1-methyl-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

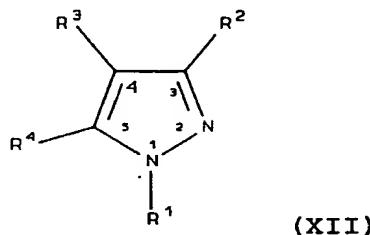
85. A compound of claim 1 that is 4-[3-(3-fluorophenyl)1-methyl-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

86. A compound of claim 1 that is 4-[3-(3-fluorophenyl)-1-methyl-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

87. A compound of claim 1 that is 5-(4-fluorophenyl)-N-2-propynyl-4-(4-pyridinyl)-1H-pyrazol-3-amine or a pharmaceutically-acceptable salt or a tautomer thereof.

88. A substituted pyrazole that specifically binds to an ATP binding site of p38 kinase.

89. A compound of claim 88 having the formula:



wherein

5 R¹ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units; and

10 R² is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical that binds with p38 kinase at said ATP binding site of p38 kinase; and

15 R³ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a hydrogen bond acceptor functionality; and

20 R⁴ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units;

provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring containing a 2-hydroxy substituent and when R¹ is hydrido; further provided R² is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R⁴ is hydrido; and further provided R⁴ is not

methylsulfonylphenyl; or
a pharmaceutically-acceptable salt or tautomer
thereof.

90. A compound of claim 89 wherein R² is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical that binds with Lys₅₂, Glu₆₉, Leu₇₃, Ile₈₂, Leu₈₄, Leu₁₀₁, and Thr₁₀₃ sidechains at said ATP binding site of p38 kinase, said radical being substantially disposed within a hydrophobic cavity formed during said binding by p38 kinase at the ATP binding site.

5 91. A compound of claim 89 wherein R³ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a hydrogen bond acceptor functionality that hydrogen bonds with the N-H backbone of Met₁₀₆ of p38 kinase.

92. A compound of claim 89 wherein R¹ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 250 atomic mass units.

93. A compound of claim 89 wherein R⁴ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 250 atomic mass units.

94. A compound of claim 89 wherein R¹ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units; and
5 R² is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical wherein said radical binds with Lys₅₂, Glu₆₉, Leu₇₃, Ile₈₂, Leu₈₄, Leu₁₀₁, and Thr₁₀₃ sidechains

at said ATP binding site of p38 kinase, said radical being substantially disposed within a hydrophobic cavity
10 formed during said binding by p38 kinase at the ATP binding site; and

R³ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a hydrogen bond acceptor functionality that hydrogen bonds with the N-H backbone
15 of Met₁₀₆ of p38 kinase; and

R⁴ is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units.

95. A compound of claim 94 wherein R¹ and R⁴ are independently selected from hydrocarbyl, heterosubstituted hydrocarbyl and heterocyclyl radicals and have a combined molecular weight less than about 360
5 atomic mass units.

96. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claims 1; or a pharmaceutically acceptable salt thereof.

97. A pharmaceutical composition of Claim 96 wherein said compound is selected from the compounds of Claim 3; or a pharmaceutically acceptable salt thereof.

98. A pharmaceutical composition of Claim 96 wherein said compound is selected from the compounds of Claim 4; or a pharmaceutically acceptable salt thereof.

99. A pharmaceutical composition of Claim 96 wherein said compound is selected from the compounds of Claim 5; or a pharmaceutically acceptable salt thereof.

100. A pharmaceutical composition of Claim 96

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wherein said compound is selected from the compounds of Claim 6; or a pharmaceutically acceptable salt thereof.

101. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 24; or a pharmaceutically acceptable salt thereof.

102. A pharmaceutical composition of Claim 101 wherein said compound is selected from the compounds of Claim 25; or a pharmaceutically acceptable salt thereof.

103. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 25; or a pharmaceutically acceptable salt thereof.

104. A pharmaceutical composition of Claim 103 wherein said compound is selected from the compounds of Claim 36; or a pharmaceutically acceptable salt thereof.

105. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 44; or a pharmaceutically acceptable salt thereof.

106. A pharmaceutical composition of Claim 105 wherein said compound is selected from the compounds of Claim 45; or a pharmaceutically acceptable salt thereof.

107. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 53; or a pharmaceutically acceptable salt thereof.

108. A pharmaceutical composition of Claim 107

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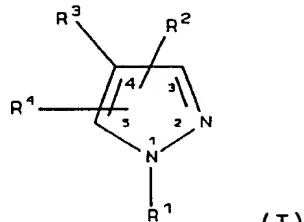
wherein said compound is selected from the compounds of Claim 54; or a pharmaceutically acceptable salt thereof.

109. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the of compounds of Claim 66; or a pharmaceutically acceptable salt thereof.

110. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claims 69; or a pharmaceutically salt thereof.

111. A pharmaceutical composition of Claim 110 wherein said compound is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

112. A method of treating a TNF mediated disorder, said method comprising treating the subject having or susceptible to such disorder with a therapeutically-effective amount of a compound of Formula I



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wherein

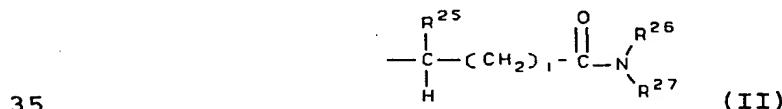
R¹ is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl,

10

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haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,
 15 heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 20 arylsulfinyl, heterocyclsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclsulfonyl, alkylaminoalkylene,
 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,
 25 heterocyclyloxycarbonylalkylene, alkoxycarbonylarylene,
 aryloxycarbonylarylene, heterocyclyloxycarbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclcarbonylarylene,
 30 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 heterocyclcarbonyloxyarylene; or

R¹ has the formula



wherein:

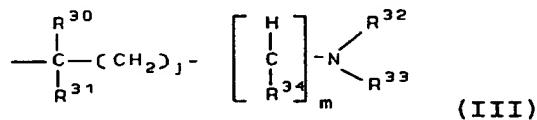
i is an integer from 0 to 9;
 R²⁵ is selected from hydrogen, alkyl, aralkyl,
 heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,
 40 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 heterocyclcarbonylaminooalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl,
alkynyl, cycloalkylalkylene, aralkyl,
45 alkoxy carbonylalkylene, and alkylaminoalkyl; and
R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
cycloalkenylalkylene, cycloalkylarylene,
cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
50 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
alkylheterocyclylalkylene, alkylheterocyclylarylene,
aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
aryloxyarylene, aralkoxyarylene,
55 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
alkoxycarbonylalkylene, alkoxy carbonyl heterocyclyl,
alkoxycarbonyl heterocyclyl carbonylalkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
60 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
arylcarbonylalkylene, alkoxy carbonylarylene,
aryloxycarbonylarylene, alkylaryloxy carbonylarylene,
arylcarbonylarylene, alkylaryl carbonylarylene,
alkoxycarbonyl heterocyclylarylene,
65 alkoxy carbonylalkoxyarylene,
heterocyclyl carbonylalkylarylene, alkylthioalkylene,
cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
70 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
75 alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
are optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,

alkoxy, keto, amino, nitro, and cyano; or
80 R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹ is selected from aralkyl, aralkoxy alkylene, heterocyclyl alkylene, alkyl heterocyclyl alkylene, alkoxy carbonyl alkylene, alkylthio alkylene, and aralkylthio alkylene; wherein said aralkyl and
85 heterocyclyl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or
 R²⁶ and R²⁷ together with the nitrogen atom to which they are attached form a heterocycle, wherein said
90 heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclyl alkylene, alkyl heterocyclyl alkylene, aryloxy alkylene, alkoxy arylene, alkyl aryloxy alkylene, alkyl carbonyl,
95 alkoxy carbonyl, aralkoxy carbonyl, alkylamino and alkoxy carbonyl amino; wherein said aryl, heterocyclyl alkylene and aryloxy alkylene radicals are optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy;
100 and
 R² is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxy alkyl, aralkyl, alkyl heterocyclyl, heterocyclyl alkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclyl amino, heterocyclyl alkyl amino, aralkyl amino, amino alkyl, amino aryl, amino alkyl amino, arylamino alkylene, alkylamino alkylene, arylamino arylene, alkylamino arylene, alkylamino alkyl amino, cycloalkyl, cycloalkenyl, alkoxy, heterocyclyloxy, alkylthio, arylthio, heterocyclylthio, carboxy, carboxy alkyl, carboxy cycloalkyl, carboxy cycloalkenyl, carboxy alkyl amino, alkoxy carbonyl, heterocyclyl carbonyl, alkoxy carbonyl alkyl, alkoxy carbonyl heterocyclyl, alkoxy carbonyl heterocyclyl carbonyl, alkoxy alkyl amino,

115 alkoxycarbonylaminoalkylamino, and heterocyclsulfonyl; wherein the aryl, heterocycl, heterocyclalkyl, cycloalkyl and cycloalkenyl groups are optionally substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, 120 aryl, heterocycl, aralkyl, heterocyclalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, 125 arylsulfonyl, and aralkylsulfonyl; or

R² has the formula:



wherein:

j is an integer from 0 to 8; and

130 m is 0 or 1; and

R³⁰ and R³¹ are independently selected from hydrogen, alkyl, aryl, heterocycl, aralkyl, heterocyclalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

135 R³² is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminalkylene;

140 R³³ is selected from hydrogen, alkyl, -C(O)R³⁵, -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵, R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocycl; and

145 R³⁴ is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

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R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy; and
 R^3 is selected from pyridinyl, pyrimidinyl,
quinolinyl, purinyl,



150

(IV)

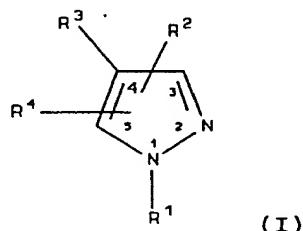
(V)

wherein R^{43} is selected from hydrogen, alkyl,
aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;
and

- 155 wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl and
purinyl groups are optionally substituted with one or
more radicals independently selected from halo, alkyl,
aralkyl, aralkenyl, arylheterocyclyl, carboxy,
carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
aralkoxy, heterocyclalkoxy, amino, alkylamino,
alkenylamino, alkynylamino, cycloalkylamino,
cycloalkenylamino, arylamino, heterocyclylamino,
aminocarbonyl, cyano, hydroxy, hydroxyalkyl,
165 alkoxycarbonyl, aryloxycarbonyl, heterocyclloxy carbonyl,
alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl,
aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino,
aralkylamino, heterocyclalkylamino,
aralkylheterocyclylamino, nitro, alkylaminocarbonyl,
170 alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl,
alkylcarbonyl, hydrazinyl, alkylhydrazinyl,
arylhydrazinyl, or $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or
amino, and R^{45} is alkyl or aralkyl; and
- 175 R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals

independently selected from halo, alkyl, alkenyl,
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
 180 alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 185 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;
 provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring
 containing a 2-hydroxy substituent and when R¹ is hydrido;
 further provided R² is selected from aryl, heterocyclyl,
 190 unsubstituted cycloalkyl and cycloalkenyl when R⁴ is
 hydrido; and further provided R⁴ is not
 methylsulfonylphenyl; or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

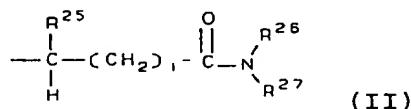
113. A method of treating a p38 kinase mediated disorder, said method comprising treating the subject having or susceptible to such disorder with a therapeutically-effective amount of a compound of
 5 Formula I



wherein

R¹ is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl,

- 10 cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 arylheterocycl, carboxy, carboxyalkyl, alkoxyalkyl,
 15 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,
 heterocyclyoxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 alkenylamino, alkynylamino, arylamino, heterocyclamino,
 20 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclsulfonyl, alkylaminoalkylene,
 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 25 alkoxy carbonylalkylene, aryloxycarbonylalkylene,
 heterocycloxycarbonylalkylene, alkoxy carbonylarylene,
 aryloxycarbonylarylene, heterocycloxycarbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclcarbonylalkylene, alkylcarbonylarylene,
 30 arylcarbonylarylene, heterocyclcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 heterocyclcarbonyloxyarylene; or
- 35 R¹ has the formula .



wherein:

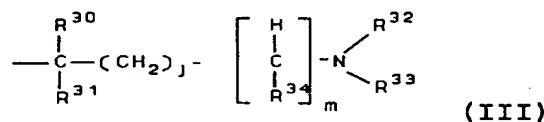
- i is an integer from 0 to 9;
 R²⁵ is selected from hydrogen, alkyl, aralkyl,
 40 heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,

alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclycarbonylaminoalkylene; and R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxy carbonylalkylene, alkoxy carbonyl heterocyclyl, alkoxy carbonyl heterocyclyl carbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylamino carbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, alkylaryloxy carbonylarylene, arylcarbonylarylene, alkylaryl carbonylarylene, alkoxy carbonyl heterocyclylarylene, alkoxy carbonylalkoxyarylene, heterocyclyl carbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, aralkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylheterocyclylarylene, alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene, aryloxy carbonylarylene, arylcarbonylarylene, alkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, and alkylsulfonylarylene groups

are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl,
80 alkoxy, keto, amino, nitro, and cyano; or
R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹ is selected from aralkyl, aralkoxy alkylene, heterocyclyl alkylene, alkyl heterocyclyl alkylene, alkoxy carbonyl alkylene, alkylthio alkylene, and aralkylthio alkylene; wherein said aralkyl and heterocyclyl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or
R²⁶ and R²⁷ together with the nitrogen atom to which they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclyl alkylene, alkyl heterocyclyl alkylene, aryloxy alkylene,
95 alkoxy arylene, alkyl aryloxy alkylene, alkyl carbonyl, alkoxy carbonyl, aralkoxy carbonyl, alkyl amino and alkoxy carbonyl amino; wherein said aryl, heterocyclyl alkylene and aryloxy alkylene radicals are optionally substituted with one or more radicals
100 independently selected from halogen, alkyl and alkoxy; and
R² is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxy alkyl, aralkyl, alkyl heterocyclyl, heterocyclyl alkyl, alkyl amino, alkenyl amino, alkynyl amino, aryl amino, heterocyclyl amino, heterocyclyl alkyl amino, aralkyl amino, amino alkyl, amino aryl, amino alkyl amino, aryl amino alkylene, alkyl amino alkylene, aryl amino arylene, alkyl amino arylene, alkyl amino alkyl amino, cycloalkyl,
105 cycloalkenyl, alkoxy, heterocyclyloxy, alkylthio, arylthio, heterocyclylthio, carboxy, carboxy alkyl, carboxy cycloalkyl, carboxy cycloalkenyl, carboxy alkyl amino, alkoxy carbonyl, heterocyclyl carbonyl,

115 alkoxy carbonylalkyl, alkoxy carbonyl heterocyclyl,
 alkoxy carbonyl heterocyclyl carbonyl, alkoxy alkylamino,
 alkoxy carbonyl aminoalkylamino, and heterocyclylsulfonyl;
 wherein the aryl, heterocyclyl, heterocyclylalkyl,
 cycloalkyl and cycloalkenyl groups are optionally
 substituted with one or more radicals independently
 120 selected from halo, keto, amino, alkyl, alkenyl, alkynyl,
 aryl, heterocyclyl, aralkyl, heterocyclylalkyl,
 epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,
 aralkoxy, haloalkyl, alkylamino, alkynylamino,
 alkylaminoalkylamino, heterocyclylalkylamino,
 125 alkylcarbonyl, alkoxy carbonyl, alkylsulfonyl,
 arylsulfonyl, and aralkylsulfonyl; or

R² has the formula:

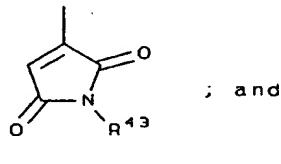


wherein:

130 j is an integer from 0 to 8; and
 m is 0 or 1; and
 R³⁰ and R³¹ are independently selected from hydrogen,
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,
 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,
 135 alkoxyalkyl, and alkylcarbonyloxyalkyl; and
 R³² is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 140 heterocyclylcarbonylaminooalkylene;
 R³³ is selected from hydrogen, alkyl, -C(O)R³⁵,
 -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵,
 R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from
 hydrocarbon, heterosubstituted hydrocarbon and
 145 heterocyclyl; and

R³⁴ is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or R² is -CR⁴¹R⁴² wherein R⁴¹ is aryl, and R⁴² is hydroxy; and R³ is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,

150



(IV)

(V)

wherein R⁴³ is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;

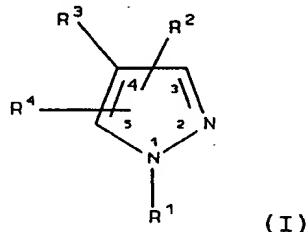
155 and

wherein the R³ pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxycarbonyl, aryloxycarbonyl, heterocycloxycarbonyl, alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, heterocyclalkylamino, aralkylheterocyclamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, or -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or amino, and R⁴⁵ is alkyl or aralkyl; and

175 R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,

cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R⁴ is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy; provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring containing a 2-hydroxy substituent and when R¹ is hydrido; further provided R² is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R⁴ is hydrido; and further provided R⁴ is not methylsulfonylphenyl; or a pharmaceutically-acceptable salt or tautomer thereof.

114. A method of treating inflammation, said method comprising treating the subject having or susceptible to inflammation with a therapeutically-effective amount of a compound of Formula I



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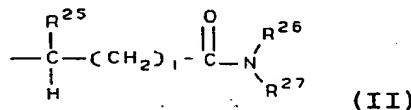
wherein

R¹ is selected from hydrido, alkyl, cycloalkyl,

794

alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl,
 cycloalkylalkylene, cycloalkenylalkylene,
 10 heterocyclylalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,
 15 heterocycloloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 20 arylsulfinyl, heterocyclsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclsulfonyl, alkylaminoalkylene,
 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxy carbonylalkylene, aryloxy carbonylalkylene,
 25 heterocycloloxy carbonylalkylene, alkoxy carbonylarylene,
 aryloxy carbonylarylene, heterocycloloxy carbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclcarbonylarylene,
 30 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 heterocyclcarbonyloxyarylene; or

R¹ has the formula



35

wherein:

i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl,
 heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,

SUBSTITUTESHEET (RULE 26)

40 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
alkylcarbonylalkylene, arylcarbonylalkylene, and
heterocyclcylcarbonylaminoalkylene; and
R²⁶ is selected from hydrogen, alkyl, alkenyl,
alkynyl, cycloalkylalkylene, aralkyl,
45 alkoxy carbonylalkylene, and alkylaminoalkyl; and
R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
aryl, heterocyclcyl, aralkyl, cycloalkylalkylene,
cycloalkenylalkylene, cycloalkylarylene,
cycloalkylcycloalkyl, heterocyclcylalkylene, alkylarylene,
50 alkylaralkyl, aralkylarylene, alkylheterocyclcyl,
alkylheterocyclcylalkylene, alkylheterocyclcylarylene,
aralkylheterocyclcyl, alkoxyalkylene, alkoxyarylene,
alkoxyaralkyl, alkoxyheterocyclcyl, alkoxyalkoxyarylene,
aryloxyarylene, aralkoxyarylene,
55 alkoxyheterocyclcylalkylene, aryloxyalkoxyarylene,
aloxycarbonylalkylene, aloxycarbonylheterocyclcyl,
aloxycarbonylheterocyclcylcarbonylalkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylamino carbonylalkylene, aminocarbonylalkylene,
60 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
arylcarbonylalkylene, alkoxy carbonylarylene,
aryloxycarbonylarylene, alkylaryloxy carbonylarylene,
arylcarbonylarylene, alkylarylcarbonylarylene,
aloxycarbonylheterocyclcylarylene,
65 aloxycarbonylalkoxyarylene,
heterocyclcylcarbonylalkylarylene, alkylthioalkylene,
cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclcylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
70 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclcyl, aralkyl,
heterocyclcylalkylene, alkylheterocyclcylarylene,
aloxoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
75 alkylthioarylene, heterocyclcylthioarylene,

arylthioalkylarylene, and alkylsulfonylarylene groups are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano; or

80 R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxycarbonyl, and R²⁹ is selected from aralkyl, aralkoxyalkylene, heterocyclalkylene, alkylheterocyclalkylene, alkoxycarbonylalkylene, alkylthioalkylene, and aralkylthioalkylene; wherein said aralkyl and

85 heterocycl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or

90 R²⁶ and R²⁷ together with the nitrogen atom to which they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocycl, heterocyclalkylene, alkylheterocyclalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl, heterocyclalkylene and aryloxyalkylene radicals are optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy;

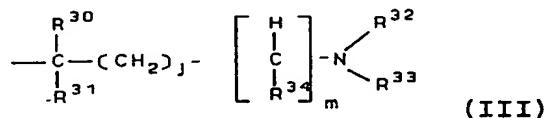
95 and

100 R² is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocycl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocycl, heterocyclalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclamino, heterocyclalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocycloxy, alkylthio, arylthio, heterocyclthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl,

797

carboxyalkylamino, alkoxycarbonyl, heterocyclcarbonyl,
alkoxycarbonylalkyl, alkoxycarbonylheterocycl,
alkoxycarbonylheterocyclcarbonyl, alkoxyalkylamino,
115 alkoxycarbonylaminoalkylamino, and heterocyclsulfonyl;
wherein the aryl, heterocycl, heterocyclalkyl,
cycloalkyl and cycloalkenyl groups are optionally
substituted with one or more radicals independently
selected from halo, keto, amino, alkyl, alkenyl, alkynyl,
120 aryl, heterocycl, aralkyl, heterocyclalkyl,
epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,
aralkoxy, haloalkyl, alkylamino, alkynylamino,
alkylaminoalkylamino, heterocyclalkylamino,
alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,
125 arylsulfonyl, and aralkylsulfonyl; or

R^2 has the formula:



wherein:

j is an integer from 0 to 8; and

130 m is 0 or 1; and

R^{30} and R^{31} are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

135 R³² is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene;

140 R³³ is selected from hydrogen, alkyl, -C(O)R³⁵, -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵, R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from hydrocarbon, heterosubstituted hydrocarbon and

heterocyclyl; and

- 145 R³⁴ is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or R² is -CR⁴¹R⁴² wherein R⁴¹ is aryl, and R⁴² is hydroxy; and R³ is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



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(IV)

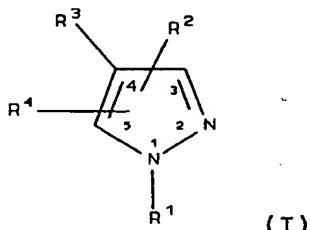
(V)

wherein R⁴³ is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

- 155 wherein the R³ pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxycarbonyl, aryloxycarbonyl, heterocyclloxy carbonyl, alkoxy carbonylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, heterocyclalkylamino, aralkylheterocyclalkylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, or -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or amino, and R⁴⁵ is alkyl or aralkyl; and

175 R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
 independently selected from halo, alkyl, alkenyl,
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
 180 alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxy carbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 185 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;
 provided R^3 is not 2-pyridinyl when R^4 is a phenyl ring
 containing a 2-hydroxy substituent and when R^1 is hydrido;
 further provided R^2 is selected from aryl, heterocyclyl,
 190 unsubstituted cycloalkyl and cycloalkenyl when R^4 is
 hydrido; and further provided R^4 is not
 methylsulfonylphenyl; or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

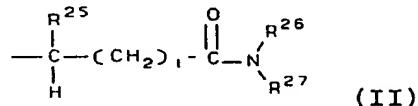
115. A method of treating arthritis, said method
 comprising treating the subject having or susceptible to
 arthritis with a therapeutically-effective amount of a
 compound of Formula I



800

wherein

R¹ is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocyclyloxy carbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, heterocyclyloxy carbonylarylene, alkyl carbonylalkylene, aryl carbonylalkylene, heterocyclyl carbonylalkylene, alkyl carbonylarylene, aryl carbonylarylene, heterocyclyl carbonyloxyalkylene, aryl carbonyloxyalkylene, and heterocyclyl carbonyloxyarylene; or

R¹ has the formula

wherein:

i is an integer from 0 to 9;

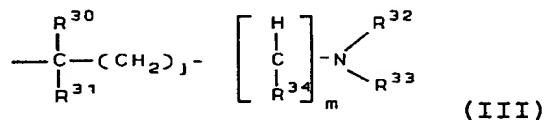
R²⁵ is selected from hydrogen, alkyl, aralkyl,
heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,
40 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
alkylcarbonylalkylene, arylcarbonylalkylene, and
heterocyclcarbonylaminoalkylene; and
R²⁶ is selected from hydrogen, alkyl, alkenyl,
alkynyl, cycloalkylalkylene, aralkyl,
45 alkoxy carbonylalkylene, and alkylaminoalkyl; and
R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
cycloalkenylalkylene, cycloalkylarylene,
50 cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene,
alkylaralkyl, aralkylarylene, alkylheterocyclyl,
alkylheterocyclalkylene, alkylheterocyclarylene,
aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
55 aryloxyarylene, aralkoxyarylene,
alkoxyheterocyclalkylene, aryloxyalkoxyarylene,
aloxycarbonylalkylene, alkoxy carbonylheterocyclyl,
aloxycarbonylheterocyclcarbonylalkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
60 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
arylcarbonylalkylene, alkoxy carbonylarylene,
aryloxycarbonylarylene, alkylaryloxy carbonylarylene,
arylcarbonylarylene, alkylarylcarbonylarylene,
aloxycarbonylheterocyclarylene,
65 aloxycarbonylalkoxyarylene,
heterocyclcarbonylalkylarylene, alkylthioalkylene,
cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
70 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
heterocyclalkylene, alkylheterocyclarylene,
aloxoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,

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aryloxycarbonylarylene, arylcarbonylarylene,
75 alkylthioarylene, heterocyclthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
are optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or
80 R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹
is selected from aralkyl, aralkoxyalkylene,
heterocyclalkylene, alkylheterocyclalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
85 heterocycyl groups are optionally substituted with one
or more radicals independently selected from alkyl and
nitro; or
R²⁶ and R²⁷ together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
90 heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
heterocycl, heterocyclalkylene,
alkylheterocyclalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
95 alkoxy carbonyl, aralkoxy carbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
heterocyclalkylene and aryloxyalkylene radicals are
optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
100 and
R² is selected from hydrido, halogen, alkyl, alkenyl,
alkynyl, aryl, heterocycl, haloalkyl, hydroxyalkyl,
aralkyl, alkylheterocycl, heterocyclalkyl,
alkylamino, alkenylamino, alkynylamino, arylamino,
105 heterocyclamino, heterocyclalkylamino, aralkylamino,
aminoalkyl, aminoaryl, aminoalkylamino,
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,
alkylaminoaryl ene, alkylaminoalkylamino, cycloalkyl,
cycloalkenyl, alkoxy, heterocycloxy, alkylthio,

110 arylthio, heterocyclylthio, carboxy, carboxyalkyl,
 carboxycycloalkyl, carboxycycloalkenyl,
 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,
 alkoxy carbonylalkyl, alkoxy carbonylheterocyclyl,
 alkoxy carbonylheterocyclylcarbonyl, alkoxyalkylamino,
 115 alkoxy carbonylaminoalkylamino, and heterocyclylsulfonyl;
 wherein the aryl, heterocyclyl, heterocyclylalkyl,
 cycloalkyl and cycloalkenyl groups are optionally
 substituted with one or more radicals independently
 selected from halo, keto, amino, alkyl, alkenyl, alkynyl,
 120 aryl, heterocyclyl, aralkyl, heterocyclylalkyl,
 epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,
 aralkoxy, haloalkyl, alkylamino, alkynylamino,
 alkylaminoalkylamino, heterocyclylalkylamino,
 alkylcarbonyl, alkoxy carbonyl, alkylsulfonyl,
 125 arylsulfonyl, and aralkylsulfonyl; or

R² has the formula:



wherein:

j is an integer from 0 to 8; and
 130 m is 0 or 1; and
 R³⁰ and R³¹ are independently selected from hydrogen,
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,
 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and
 135 R³² is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 heterocyclylcarbonylaminoalkylene;
 140 R³³ is selected from hydrogen, alkyl, -C(O)R³⁵,
 -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵,

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R^{36} , R^{37} , R^{38} , R^{39} and R^{40} are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

- 145 R^{34} is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or
 R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy; and
 R^3 is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



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(IV)

(V)

wherein R^{43} is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

- 155 wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxycarbonyl, aryloxycarbonyl, heterocycloxycarbonyl, alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, heterocyclalkylamino, aralkylheterocyclamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl,

arylhydrazinyl, or -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or amino, and R⁴⁵ is alkyl or aralkyl; and

175 R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R⁴ is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

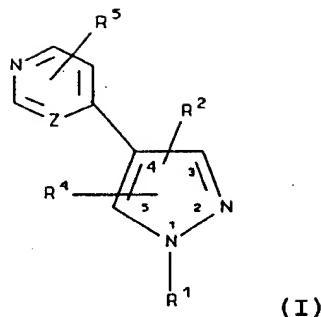
180 alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy;

185 provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring containing a 2-hydroxy substituent and when R¹ is hydrido; further provided R² is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R⁴ is hydrido; and further provided R⁴ is not methylsulfonylphenyl; or

190 a pharmaceutically-acceptable salt or tautomer thereof.

116. A method of treating a p38 kinase mediated disorder, said method comprising treating the subject having or susceptible to such disorder with a therapeutically-effective amount of a compound of
5 Formula I

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wherein

- Z represents a carbon atom or a nitrogen atom; and
- R¹ is selected from hydrido, lower alkyl, lower hydroxyalkyl and lower alkynyl; and
- 10 R² is selected from hydrido and lower alkyl; and
- R⁴ is selected from phenyl and benzodioxolyl; wherein phenyl is optionally substituted with one or more halo radicals; and
- 15 R⁵ is selected from hydrido, halo and alkylhydrazinyl; or
- a pharmaceutically-acceptable salt or tautomer thereof.

- 117. The method of Claim 112 wherein the TNF mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid
- 5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,
- 10 inflammatory bowel disease and cachexia.

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118. The method of Claim 112 wherein the TNF mediated disorder is inflammation.

119. The method of Claim 112 wherein the TNF mediated disease is arthritis.

120. The method of Claim 112 wherein the TNF mediated disorder is asthma.

121. The method of claim 112 wherein the compound is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

122. The method of claim 112 wherein the compound is 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine or a pharmaceutically-acceptable salt or a tautomer thereof.

123. The method of Claim 113 wherein the disorder is a p38 α kinase mediated disorder.

124. The method of Claim 113 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis, 10 inflammatory bowel disease and cachexia.

125. The method of Claim 113 wherein the p38 kinase mediated disorder is inflammation.

126. The method of Claim 113 wherein the p38 kinase

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mediated disorder is arthritis.

127. The method of Claim 113 wherein the p38 kinase mediated disorder is asthma.

128. The method of Claim 116 wherein the disorder is a p38 α kinase mediated disorder.

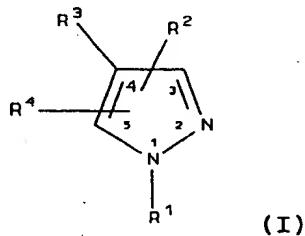
129. The method of Claim 116 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid 5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis, 10 inflammatory bowel disease and cachexia.

130. The method of Claim 116 wherein the p38 kinase mediated disorder is inflammation.

131. The method of Claim 116 wherein the p38 kinase mediated disorder is arthritis.

132. The method of Claim 116 wherein the p38 kinase mediated disorder is asthma.

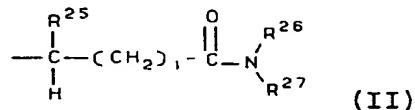
133. A method of preparing pyrazoles of Formula I



wherein

- R¹ is selected from hydrido, alkyl, cycloalkyl,
 5 alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl,
 cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclylalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,
 heterocycloloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclsulfonyl, alkylaminoalkylene,
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxy carbonylalkylene, aryloxycarbonylalkylene,
 heterocycloloxy carbonylalkylene, alkoxy carbonylarylene,
 aryloxycarbonylarylene, heterocycloloxy carbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 25 heterocyclcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 30 heterocyclcarbonyloxyarylene; or

R¹ has the formula



wherein:

i is an integer from 0 to 9;

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35 R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene; and

40 R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and

 R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene,

45 cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl, alkoxyalkylene, alkoxyarylene,

50 alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxy carbonylalkylene, alkoxy carbonylheterocycl, alkoxy carbonylheterocyclcarbonylalkylene, aminoalkyl,

55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxy carbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene,

60 arylcarbonylarylene, alkylarylcarbonylarylene, alkoxy carbonylheterocyclarylene, alkoxy carbonylalkoxylarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

65 aralkylthioarylene, heterocyclthioarylene, arylthioalkylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocycl, aralkyl, heterocyclalkylene, alkylheterocyclarylene,

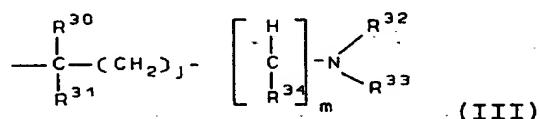
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,

aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclithioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
are optionally substituted with one or more radicals
75 independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or
R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹
is selected from aralkyl, aralkoxyalkylene,
heterocyclalkylene, alkylheterocyclalkylene,
80 alkoxy carbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocycl groups are optionally substituted with one
or more radicals independently selected from alkyl and
nitro; or
85 R²⁶ and R²⁷ together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
heterocycl, heterocyclalkylene,
90 alkylheterocyclalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
heterocyclalkylene and aryloxyalkylene radicals are
95 optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and
R² is selected from hydrido, halogen, alkyl, alkenyl,
100 alkynyl, aryl, heterocycl, haloalkyl, hydroxyalkyl,
aralkyl, alkylheterocycl, heterocyclalkyl,
alkylamino, alkenylamino, alkynylamino, arylamino,
heterocyclamino, heterocyclalkylamino, aralkylamino,
aminoalkyl, aminoaryl, aminoalkylamino,
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,
105 alkylaminoarylene, alkylaminoalkylamino, cycloalkyl,
cycloalkenyl, alkoxy, heterocyclxyo, alkylthio,

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arylthio, heterocyclylthio, carboxy, carboxyalkyl,
carboxycycloalkyl, carboxycycloalkenyl,
carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,
110 alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl,
alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
alkoxycarbonylaminooalkylamino, and heterocyclylsulfonyl;
wherein the aryl, heterocyclyl, heterocyclylalkyl,
cycloalkyl and cycloalkenyl groups are optionally
115 substituted with one or more radicals independently
selected from halo, keto, amino, alkyl, alkenyl, alkynyl,
aryl, heterocyclyl, aralkyl, heterocyclylalkyl,
epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,
aralkoxy, haloalkyl, alkylamino, alkynylamino,
120 alkylaminoalkylamino, heterocyclylalkylamino,
alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,
arylsulfonyl, and aralkylsulfonyl; or

R^2 has the formula:



125 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

R³⁰ and R³¹ are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

R³² is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

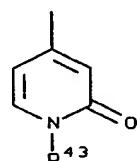
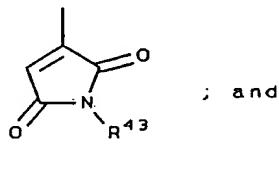
R^{33} is selected from hydrogen, alkyl, $-C(O)R^{35}$, $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$, wherein R^{35} ,

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140 R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

R³⁴ is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

145 R² is -CR⁴¹R⁴² wherein R⁴¹ is aryl, and R⁴² is hydroxy; and R³ is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



(IV)

(V)

150 wherein R⁴³ is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

155 wherein the R³ pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxycarbonyl, aryloxycarbonyl, heterocyclloxycarbonyl, alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, heterocyclalkylamino, aralkylheterocyclamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl,

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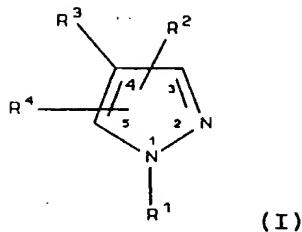
arylhydrazinyl, or -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or
170 amino, and R⁴⁵ is alkyl or aralkyl; and
R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
R⁴ is optionally substituted with one or more radicals
independently selected from halo, alkyl, alkenyl,
175 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
180 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy; or
a pharmaceutically-acceptable salt or tautomer
185 thereof,
said method comprising the steps of forming an acyl
hydrazone and condensing to form the substituted
pyrazole.

134. The process of Claim 133 wherein the acyl
hydrazone is formed by reaction of a ketone with an acyl
hydrazide.

135. The process of Claim 133 wherein the
condensation is performed at a temperature from about 25
°C to about 200 °C.

136. A method of preparing pyrazoles of Formula I

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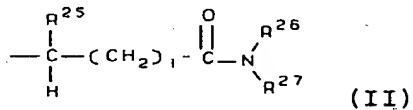


wherein

- R¹ is selected from hydrido, alkyl, cycloalkyl,
- 5 alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
- 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, heterocycloloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino,
- 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclsulfonyl, alkylaminoalkylene,
- 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxy carbonylalkylene, aryloxycarbonylalkylene, heterocycloxycarbonylalkylene, alkoxy carbonylarylene, aryloxycarbonylarylene, heterocycloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene,
- 25 heterocyclcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and

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- 30 heterocyclcarbonyloxyarylene; or
 R¹ has the formula



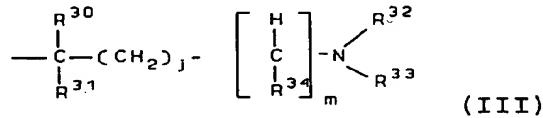
wherein:

- i is an integer from 0 to 9;
 35 R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene; and
 40 R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and
 R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene,
 45 cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocycl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxy carbonylalkylene, alkoxy carbonylheterocycl, alkoxy carbonylheterocyclcarbonylalkylene, aminoalkyl,
 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylamino carbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxy carbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene, arylcarbonylarylene, alkylaryl carbonylarylene, alkoxy carbonylheterocyclarylene,

alkoxycarbonylalkoxylarylene,
heterocyclcarbonylalkylarylene, alkylthioalkylene,
cycloalkylthioalkylene, alkylthioarylene,
65 aralkylthioarylene, heterocyclthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocycl, aralkyl,
heterocyclalkylene, alkylheterocyclarylene,
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
are optionally substituted with one or more radicals
75 independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or
R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxy carbonyl, and R²⁹
is selected from aralkyl, aralkoxyalkylene,
heterocyclalkylene, alkylheterocyclalkylene,
80 alkoxy carbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocycl groups are optionally substituted with one
or more radicals independently selected from alkyl and
nitro; or
85 R²⁶ and R²⁷ together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
heterocycl, heterocyclalkylene,
90 alkylheterocyclalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
heterocyclalkylene and aryloxyalkylene radicals are
95 optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and

R² is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, 100 aralkyl, alkylheterocyclyl, heterocyclalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclalamino, heterocyclalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, 105 alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocycloxy, alkylthio, arylthio, heterocyclthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclcarbonyl, 110 alkoxycarbonylalkyl, alkoxycarbonylheterocycl, alkoxycarbonylheterocyclcarbonyl, alkoxyalkylamino, alkoxycarbonylaminoalkylamino, and heterocyclsulfonyl; wherein the aryl, heterocyclyl, heterocyclalkyl, cycloalkyl and cycloalkenyl groups are optionally 115 substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, 120 alkylaminoalkylamino, heterocyclalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, arylsulfonyl, and aralkylsulfonyl; or

R² has the formula:



125 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

R³⁰ and R³¹ are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene,

- 130 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,
alkoxyalkyl, and alkylcarbonyloxyalkyl; and
R³² is selected from hydrogen, alkyl, aralkyl,
heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
135 alkylcarbonylalkylene, arylcarbonylalkylene, and
heterocyclcarbonylaminoalkylene;
R³³ is selected from hydrogen, alkyl, -C(O)R³⁵,
-C(O)OR³⁶, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵,
R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from
140 hydrocarbon, heterosubstituted hydrocarbon and
heterocycl; and
R³⁴ is selected from hydrogen, alkyl, aminocarbonyl,
alkylaminocarbonyl, and arylaminocarbonyl; or
R² is -CR⁴¹R⁴² wherein R⁴¹ is aryl, and R⁴² is hydroxy; and
145 R³ is selected from pyridinyl, pyrimidinyl,
quinolinyl, purinyl,



(IV)

(V)

- 150 wherein R⁴³ is selected from hydrogen, alkyl,
aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;
and
wherein the R³ pyridinyl, pyrimidinyl, quinolinyl and
purinyl groups are optionally substituted with one or
more radicals independently selected from halo, alkyl,
155 aralkyl, aralkenyl, arylheterocycl, carboxy,
carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
aralkoxy, heterocyclalkoxy, amino, alkylamino,
alkenylamino, alkynylamino, cycloalkylamino,

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160 cycloalkenylamino, arylamino, heterocyclylamino,
aminocarbonyl, cyano, hydroxy, hydroxyalkyl,
alkoxycarbonyl, aryloxycarbonyl, heterocyclloxycarbonyl,
alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl,
aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino,
165 aralkylamino, heterocyclalkylamino,
aralkylheterocyclylamino, nitro, alkylaminocarbonyl,
alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl,
alkylcarbonyl, hydrazinyl, alkylhydrazinyl,
arylhydrazinyl, or -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or
170 amino, and R⁴⁵ is alkyl or aralkyl; and
 R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R⁴ is optionally substituted with one or more radicals
 independently selected from halo, alkyl, alkenyl,
175 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
 alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
180 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy; or
 a pharmaceutically-acceptable salt or tautomer
185 thereof,
 said method comprising the steps of treating a
 substituted ketone with an acyl hydrazide to give the
 pyrazole.

137. The process of Claim 136 wherein it is carried out in an acidic solvent.

138. The process of Claim 137 wherein the acidic solvent is acetic acid.

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139. The process of Claim 137 wherein the acidic solvent is an organic solvent containing an acid.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/10436

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D401/04	A61K31/415	A61K31/44	A61K31/505	C07D401/14
C07D409/14	C07D413/14	C07D405/14	C07D471/04	C07D417/14
C07D453/02 // (C07D471/04, 237:00, 231:00), (C07D471/04, 237:00,				

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 03385 A (SEARLE & CO ;LEE LEN F (US); PENNING THOMAS D (US); KRAMER STEVEN) 8 February 1996 cited in the application see abstract; claims 1,8,10 see page 10 - page 13 see page 17 see page 24 - page 26 see page 41 - page 44 ---	1-139
X	US 5 559 137 A (ADAMS JERRY L ET AL) 24 September 1996 cited in the application see abstract; claim 1; example 1 ---	1-139 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- "&" document member of the same patent family

Date of the actual completion of the international search

11 September 1998

Date of mailing of the international search report

24/09/1998

Name and mailing address of the ISA

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Authorized officer

Paisdor, B

INTERNATIONAL SEARCH REPORT

In ntional Application No
PCT/US 98/10436

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 233:00)

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A X	CATIVIELA C ET AL: "On the synthesis of 3(5)-(carbomethoxy)-4-hetarylpyrazoles" J. HETEROCLYL. CHEM. (JHTCAD, 0022152X);88; VOL.25 (3); PP.851-5, XP002077334 Univ. Zaragoza; Inst. Cienc. Mater. Aragon; Zaragoza; 50009; Spain (ES) see page 851; examples 3E,3F,4E,4F see page 854	1-3, 9-11,15, 16,20,21 88-95 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

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- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "S" document member of the same patent family

Date of the actual completion of the international search

11 September 1998

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/US 98/10436

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FISCHER U ET AL: "1,3-Dipolar additions to 7-methylthieno'2,3-c!pyridine 1,1-dioxide" HELV. CHIM. ACTA (HCACAV,0018019X);80; VOL.63 (6); PP.1719-27, XP002077335 F. Hoffmann-La Roche und Co., A.-G.;Pharm. Forschungsabt.; Basel; CH-4002; Switz. see page 1719; example 4 see page 1720; examples 10,13 see page 1721; examples 16,17,19,20	1-5, 9-11, 15-22
X		88-95
A	CHEMICAL ABSTRACTS, vol. 098, no. 1, 3 January 1983 Columbus, Ohio, US; abstract no. 004498. POPOVA A N ET AL: "Synthesis of 4-(pyrazol-4-yl)-substituted salts of pyrylium and pyridines" XP002077337 see abstract	1-3, 9-11,15, 16,20,21
X	& KHIM. GETEROTSIKL. SOEDIN. (KGSSAQ,04538234);82; (9); PP.1280, Rostov. Gos. Univ.;Rostov-on-Don; 344006; USSR (SU) ---	88-95
A	BAUER V J ET AL: "4-'3(5)-Pyrazolyl!pyridinium salts. A new class of hypoglycemic agents" J. MED. CHEM. (JMCMAR);68; VOL.11 (5); PP.981-4, XP002077336 Div. of Amer. Cyanamid Co.;Lederle Lab.; Pearl River; N. Y. see page 981; examples 1-5 see page 982; table I see page 983; table II	1-3, 9-11,15, 16,20,21
X	-----	88-95

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/10436

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 112-132 because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 112-132 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking(Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In International Application No
PCT/US 98/10436

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9603385 A	08-02-1996	US 5486534 A		23-01-1996
		AU 3126795 A		22-02-1996
		CA 2195123 A		08-02-1996
		EP 0772597 A		14-05-1997
		JP 10503201 T		24-03-1998
		US 5580985 A		03-12-1996
		US 5756530 A		26-05-1998
US 5559137 A	24-09-1996	JP 10500413 T		13-01-1998
		WO 9531451 A		23-11-1995